http://wapo.st/2bNUkHU

As Congo's globe-threatening yellow fever pandemic explodes, they ask 'where is the vaccine?'

Here in Kinshasa they're using bug spray to repel a pandemic.

By Emily J. Baumgaertner August 22 at 3:00 AM

KINSHASA, Congo - At first glance, it looks like a bloody ambush on civilians: dozens in uniform are storming into a bustling marketplace bearing on their shoulders what look like bazookas.

People are screaming, scrambling in every direction, their noses and mouths covered as they drag their children by their hands. Those in uniform chuckle, shaking their heads, smirking; they hiss into megaphones: "We told you we were coming!"

This is vector control in Kinshasa, the capital of the Congo.

The procedure daubs communities in insecticide to fumigate homes and public spaces that breed Aedes aegypti, the mosquito carrying yellow fever. In high quantities, the insecticide is a neurotoxin, and the health workers lament that marketplace invasions seem most petrifying for locals because "there's nowhere for people to hide."

The method, a poor alternative to vaccination, is being implemented in the fight against central Africa's yellow fever outbreak, which has surpassed 6100 suspected cases in Angola and the Congo killing at least 400 without slowing.

After a sluggish and disorderly outbreak response (vanishing vaccines, unrefrigerated vaccines, and ultimately, a four-time global depletion of vaccines), authorities seem to leisurely await the virus's explosion into Asia and beyond. For months, this bug-spraying protocol has been the only thing keeping aid workers occupied as they wait for 15.5 million more vaccines from higher-ups — vaccines that never seem to come.

Yellow fever is a preventable killer without a cure. The infection shows itself with flu-like symptoms: fever, chills, nausea and vomiting. Most immune systems can fight off the infection over time, but around 15 percent of cases develop jaundice, bleeding from the mouth and nose, and/or eventual organ failure.Aside from support measures like fluid and oxygen, there is no treatment for yellow fever. Up to half of severe cases die. Unlike Zika (or Ebola, and other re-emerging threats), there already exists a yellow fever vaccine — one that's cheap, lifelong, and highly efficacious.But advancements in the yellow fever approach plateaued almost seven decades ago, when success against the infection suppressed transmission — and concern.

In December 2015, only four factories were producing the yellow fever vaccine globally, each employing an 80-year-old manual production process requiring 18 months from seed virus to agency approval. The entire global stockpile contained just six million vaccines.

The December 2015 yellow fever outbreak arose in the midst of the perfect storm. In the months prior, dropping oil prices for Africa's second largest crude exporter, Angola, ushered in cuts in public sanitation services; in turn, urban trash buildup created an optimal breeding ground for the mosquitoes.

It arose at the onset of the rainy season, which meant more stagnant water in old tires and stray bottle caps, where mosquitoes breed.

And most of all, it arose while the world was turned the other way, frenzied by the new epidemic, Zika.

When the outbreak sprang up in Angola, response Plan A, we'll call it, was to use the global vaccine stockpile. According to the WHO, the stockpile is intended to rapidly vaccinate each close contact surrounding a confirmed yellow fever case, thus creating a wall of immunity to smother transmission. If used correctly, six million doses are plenty.

But in this outbreak, the first cases were mistaken for food poisoning from an ethnic restaurant, and by the time Angola alerted international authorities, transmission was out of control.

Plan B, then, was the country's suggested approach: to blanket-vaccinate. In the early months of 2016, 20 million doses from around the world poured into Angola, then drained in a haphazard mass

vaccination campaign. During distribution, at least a million vaccines went missing, and of those accounted for, many were inadequately refrigerated or arrived without proper syringes.

"So, when folks say there are 'not enough vaccines,' the question is, not enough for what?" asks Bruce Aylward, ad interim executive director of WHO's Outbreaks and Health Emergencies Cluster."Yes, there was enough to identify every transmission chain [early on] and vaccinate around it. But, when countries decide that, rather than do that, let's just vaccinate this many million … then, well, no, there isn't enough."

And because there wasn't enough, the virus began skulking over the border into Congo. It was clear what would happen if the outbreak reached their unvaccinated capital.

Kinshasa, with 11.5 million people, is twice as big as Luanda, and is particularly globally connected. An outbreak on the outskirts of the urban area would be sad, but one in the midst of Kinshasa's bustle would be catastrophic. And it was.

So now, it's on to Plan C: Bug spray.

On the ground, bug spray is keeping teams busy. In addition to marketplace fumigation raids, aid workers are following orders to carry out three other types of vector control: the first is residual spraying, the application of similar insecticide against the interior walls of homes, hospitals, and schools where confirmed cases have traveled while sick.

The rationale is that the A. aegypti mosquito doesn't fly further than a 100 meter radius from its birthplace, so it often hides in the structure or compound in which it was born — and the one in which it will bite one active case and in turn transmit to a new host.

Secondly, for water reservoirs that cannot be destroyed or covered, vector control workers apply a biological agent called VectoBac. Mosquito larvae in the reservoir eat the bacteria, which then crystallizes inside of them — virtually causing the larvae to explode from the inside out.

And lastly, the teams spend enormous amounts of time doing what experts call "mechanical destruction" — a fancy term for knocking over buckets, iron cans, even littered bottle caps — anything that could serve as potential mosquito breeding grounds. The task is particularly futile in a developing metropolis like Kinshasa, where roads are spattered with garbage and every structure is crowned with hundreds of cratered concrete blocks that pool rainwater.

And at this point in an outbreak, many argue the technique is more of a handy distraction, a way to seem busy in the eyes of the desperate Congolese. Vector control is an important public health development, but all experts concur that when it comes to halting a major outbreak's transmission, the method is nowhere near as effective as vaccination.

Even Nick Duinslaeger, the director of Doctors Without Borders' (MSF) water and sanitation program for Kinshasa, has doubts about the operation he is overseeing. "I would like to see some numbers. The [vector control] activities take a lot of effort, a lot of time, a lot of human resources — and I don't know if it balances out with the impact it has," Duinslaeger says, noting his views aren't necessarily those of MSF. "For me personally, the big question remains: what parts of the activity are efficient? And is all of this really helping?"

Complacency is of particular concern when an epidemiological clock is ticking. Thanks to population density, yellow fever outbreaks tend to explode when they reach urban areas. The region's last major yellow fever outbreak, which began in Nigeria in 1986, infected 116,000 people and killed 24,000 of them — more than twice the number killed in the West African Ebola epidemic. Africa's urban populations have grown tremendously since the 80s, and thus, so has the virus's playground.

In this outbreak, soon after yellow fever began spreading through the provinces of Angola, several cases were exported to Kenya and China. The latter is of utmost concern — ripe with A. aegypti mosquitoes, host monkeys, and a perfect climate, Southeast Asia's lack of yellow

fever thus far is enigmatic. When that changes, the disease will be nearly impossible to eradicate.

"There's no evidence of a [biologically] changing virus, but there's certainly evidence of a changing world," says Aylward, referring to the risks that come with increased globalization and particularly international travel. "Many people believe that yellow fever in Asia is really just a matter of time."

In fact, a yellow fever spark in any of the 100 countries with endemic dengue — also carried by the A. aegypti — could quickly explode. Few of these areas are well vaccinated, including much of central Africa, Southeast Asia, and even the eastern seaboard of Brazil.

If you wrapped a thick piece of yellow caution tape around the equator of a standard-sized classroom globe, you'd have a good sense of the major world regions at risk in this outbreak.

Critics of the WHO are crying déjà vu; they claim the current yellow fever response, though less visible, has been botched to the degree of the response to the West African Ebola epidemic — which killed over 11,000 and took two years to contain. When a WHO emergency committee on yellow fever convened in May, the group declined to deem this yellow fever outbreak a "public health emergency of international concern," or PHEIC.

Last week, the WHO announced it would meet again in late August or early September to revisit their initial verdict.

In some ways, the Congolese households seem more in tune with the threat's magnitude than the international authorities. Since the infection lingered on the border, they've been aware that vaccination is the foolproof prevention method — and they've been begging for vaccines. When vector control teams move down each road, parcel-by-parcel, perforating water containers, residents ask: if you could make the journey here, why couldn't the vaccines make it with you?

"The main concern is vaccination, now more than ever. Everywhere we go, they are always asking, 'where is the vaccine? Where is the vaccine?'" says Ir Nobikana Nganabo Esperance, a health promoter employed by the Congo Ministry of Environment. She travels with a vector control team to sensitize locals. "We're trying to explain to them that it will come eventually. We tell them that this step 'comes first,' I guess, and afterward, maybe the government will think about vaccination."

And yes, they're thinking about it. Last Wednesday, eight months after the start of the outbreak, a $34 million dollar vaccination effort just began to roll out. The campaign will vaccinate another 15.5 million people — totaling close to 30 million — many of whom will receive only one-fifth of a dose to stretch the limited supply. Fractional doses will require a particularly small syringe, of which there is also a shortage. The massive campaign needs to be completed in less than three weeks to make sure recipients develop immunity by the end of September, when the rainy season will cause mosquito breeding to soar.

"Complacency sets in super fast," Aylward of WHO admits. "So we're trying to use this August, this small window, to belt this thing incredibly hard, raise awareness, and manage what could be a substantive international health risk."

To most, the scope, timing, and manpower required of the undertaking seem unrealistic. In most communities, it remains an ominous waiting game: the Congolese are told to hang tight, to literally kick the bucket — and to dodge response teams with their bazookas full of insecticide.

Some facts about Yellow Fever from the World Health Organization

Yellow fever is an acute viral hemorrhagic disease transmitted by infected mosquitoes. The "yellow" in the name refers to the jaundice that affects some patients.

Symptoms of yellow fever include fever, headache, jaundice, muscle pain, nausea, vomiting and fatigue.

A small proportion of patients who contract the virus develop severe symptoms and approximately half of those die within 7 to 10 days.

The virus is endemic in tropical areas of Africa and Central and South America.

Since the launch of the Yellow Fever Initiative in 2006, significant progress in combating the disease has been made in West Africa and more than 105

million people have been vaccinated in mass campaigns. No outbreaks of yellow fever were reported in West Africa during 2015.

Large epidemics of yellow fever occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes transmit the virus from person to person.

Yellow fever is prevented by an extremely effective vaccine, which is safe and affordable. A single dose of yellow fever vaccine is sufficient to confer sustained immunity and lifelong protection against yellow fever disease and a booster dose of the vaccine is not needed. The vaccine provides effective immunity within 30 days for 99 percent of people vaccinated.

Good supportive treatment in hospitals improves survival rates. There is currently no specific anti-viral drug for yellow fever.

http://bit.ly/2bFtHo2

Guarana found to have higher antioxidant potential than green tea

Research conducted at the University of São Paulo's Public Health School reveals the potential of guarana in preventing cardiovascular diseases

The millions of people who consume green tea all over the world benefit from the catechins it contains. Catechins are a class of chemical compounds with anti-oxidant and anti-inflammatory properties, among other healthy ingredients. Researchers at the University of São Paulo's Public Health School (FSP-USP) have discovered that guarana (Paullinia cupana) is a worthy competitor, at least as far as catechins are concerned: the seeds of the tropical shrub, used in fizzy drinks that are among the most popular in Brazil, as well as in over-the-counter supplements, contain more than ten times the amount of catechins found in green tea.

A clinical trial with healthy human volunteers has demonstrated that guarana is a rich source of catechins, which, when properly absorbed, reduce the oxidative stress associated with the development of neurodegenerative and cardiovascular disorders, as well as diabetes, cancer, inflammation and premature aging due to cell death, among other conditions harmful to health and wellbeing.

"Guarana has always been seen above all as a stimulant, especially by the international scientific community, because of its high caffeine content. We also found few Brazilian scientific studies that seek to identify other biological effects of guarana," said Lina Yonekura, the principal investigator for this research and currently an assistant professor at Kagawa University's School of Agriculture in Japan. "This pioneering assessment of the absorption and biological effects of its catechins in human volunteers should foster interest in guarana as a functional food on the part of scientists, the market, and society in general." The paper with the results of the study is featured on the cover of the latest issue of Food & Function, published by the Royal Society of Chemistry in the United Kingdom as one of the "Hot Articles in Food & Function 2016.

The month-long study was conducted in two stages. After selecting volunteers who were healthy but slightly overweight and with a moderately elevated risk of cardiovascular disease, the researchers measured baseline parameters on the first day and evaluated the same items again on day 15 after a the implementation of a controlled diet.

The participants were then asked to take guarana at home every morning before breakfast for the next fortnight. They were given bottles containing guarana seed powder and instructed to prepare a daily drink with the contents of one bottle (3 g of guarana powder) in 300 mL of water.

This procedure ensured that each participant acted as his or her own control. The researchers compared the same volunteers' blood tests at different times to avoid the influence of variability between individuals. The acute effect of guarana was measured one hour after the participants drank the solution on day 1 and day 15. The prolonged effect was assessed after overnight fasting on the same days.

The researchers assessed the extent to which guarana affected oxidative stress markers during the two-week intervention period. They also performed a detailed study to evaluate the subjects' absorption of catechins and their metabolites, as they had found no

information in the scientific literature on the bioavailability of these compounds in guarana.

The oxidative stress markers included oxidation of low-density lipoprotein (LDL), popularly known as bad cholesterol. LDL is essential to an organism's proper functioning because it is the main particle that carries cholesterol to cells. Cholesterol is a structural component of all cell membranes and is used to manufacture steroid hormones (estrogen and testosterone). When oxidized, however, LDL causes atherosclerosis and increases the risk of cardiovascular disease.

The tests performed by Yonekura's team showed an increase in oxidation resistance of the LDL in the blood samples taken from the volunteers after they drank guarana.

They also performed a comet assay, also called single cell gel electrophoresis (SCGE), a technique for quantifying and analyzing DNA damage in individual cells due to various factors, including oxidative stress. In this case, lymphocyte DNA in blood samples taken one hour after guarana intake was less damaged than expected when submitted to an oxidizing environment, indicating the presence of anti-oxidant substances or enhanced performance of the lymphocytes' enzymatic anti-oxidant system.

"All these markers depend on the presence of catechins in the bloodstream," Yonekura said. "The improvement in the parameters we assessed was associated with a rise in the concentration of plasma catechins after guarana intake, showing that guarana was indeed responsible for this effect."

Moreover, she went on, the guarana catechins strengthened the cells' native anti-oxidant enzymes, especially glutathione peroxidase, catalase, and superoxide dismutase, which combine to convert superoxide into peroxide and finally into water, protecting cells from the oxidative damage caused by their own metabolism of outside factors.

The tests showed increased glutathione peroxidase and catalase activity both shortly after guarana ingestion and on the following day.

"These results are exciting, suggesting that the bioavailability of guarana catechins is equal to or greater than that of green tea, cocoa and chocolate catechins," Yonekura said. "In fact, their bioavailability was sufficient to have a positive effect on plasma anti-oxidant activity, protect erythrocyte DNA, reduce plasma lipid oxidation, and increase anti-oxidant enzyme activity. We hope the results lead to heightened interest in guarana as the species is native to the Amazon, and Brazil is practically the only country that produces it on a commercial scale."

http://bit.ly/2bhBPXy

Tel Aviv University research reveals how melanoma spreads to other organs in the body

Findings may lead to a cure for the deadly disease

In a landmark discovery, researchers at Tel Aviv University have unraveled the metastatic mechanism of melanoma, the most aggressive of all skin cancers.

According to a paper published today in the journal Nature Cell Biology, the scientists discovered that before spreading to other organs, a melanoma tumor sends out tiny vesicles containing molecules of microRNA. These induce morphological changes in the dermis in preparation for receiving and transporting the cancer cells. The researchers also found chemical substances that can stop the process and are therefore promising drug candidates.

"The threat of melanoma is not in the initial tumor that appears on the skin, but rather in its metastasis -- in the tumor cells sent off to colonize in vital organs like the brain, lungs, liver and bones," said research leader Dr. Carmit Levy of the Department of Human Molecular Genetics and Biochemistry at TAU's Sackler School of Medicine. "We have discovered how the cancer spreads to distant organs and found ways to stop the process before the metastatic stage."

The TAU group worked in close collaboration with Prof. Jörg D. Hoheisel and Laureen Sander at the German Cancer Research Center (DKFZ) in Heidelberg, Dr. Shoshi Greenberger at the Sheba Medical

Center at Tel HaShomer, Israel and Dr. Ronen Brenner at the Wolfson Medical Center in Holon, Israel. Lab research was led by Dr. Shani Dror of Dr. Levy's research group.

Morphological changes in the dermis

Melanoma, the most aggressive and lethal type of skin cancer, causes the death of one person every 52 minutes according to data from the Skin Cancer Foundation, and the number of diagnosed cases has been on the rise for the past three decades. Despite a range of therapies developed over the years, there is still no full remedy for this life-threatening disease. The new study proposes novel and effective methods for diagnosing and preventing this most deadly of skin cancers.

The researchers began by examining pathology samples taken from melanoma patients. "We looked at samples of early melanoma, before the invasive stage," Dr. Levy said. "To our surprise we found changes in the morphology of the dermis -- the inner layer of the skin -- that had never before been reported. Our next task was to find out what these changes were, and how they related to melanoma."

In the ensuing study, the group was able to discover and block a central mechanism in the metastasis of melanoma.

According to Dr. Levy, scientists have known for years that melanoma forms in the outer layer of the skin, the epidermis. At this early stage, the cancer is unable to send off colonizing cancer cells because it has no access to blood vessels -- the highways that carry the cells to other parts of the body. With no blood vessels present in the epidermis, the tumor first needs to contact the abundant blood vessels running through the dermis. But how was the connection made?

"We found that even before the cancer itself invades the dermis, it sends out tiny vesicles containing molecules of microRNA," Dr. Levy said. "These induce the morphological changes in the dermis in preparation for receiving and transporting the cancer cells. It then became clear to us that by blocking the vesicles, we might be able to stop the disease altogether."

Transforming melanoma into a nonthreatening illness

Having discovered the mechanism, the researchers proceeded to look for substances that could intervene and block the process in its earliest stages. They found two such chemicals: one (SB202190) inhibits the delivery of the vesicles from the melanoma tumor to the dermis; and the other (U0126) prevents the morphological changes in the dermis even after the arrival of the vesicles. Both substances were tested successfully in the lab, and may serve as promising candidates for future drugs. In addition, the changes in the dermis, as well as the vesicles themselves, can be used as powerful indicators for early diagnosis of melanoma.

"Our study is an important step on the road to a full remedy for the deadliest skin cancer," said Dr. Levy. "We hope that our findings will help turn melanoma into a nonthreatening, easily curable disease."

http://bit.ly/2beU1XL

UTMB researchers protect against lethal Ebola Sudan infection four days after infection

Nonhuman primates protected against Ebola Sudan four days following exposure to the virus

Researchers at The University of Texas Medical Branch at Galveston, in collaboration with Arbutus Biopharma Corporation, have protected nonhuman primates against Ebola Sudan four days following exposure to the virus. The study results, which were recently published in Nature Microbiology, demonstrated that the treatment was effective at a point when animals have detectable levels of the virus in their system and were at an advanced stage of disease.

"This is a key step in our efforts to protect people from this terrible, lethal disease," said Thomas Geisbert, UTMB professor of microbiology and immunology. "The Ebola virus has five different species and will continue to impact people throughout the African continent, unfortunately with a high mortality rate."

Geisbert noted that significant progress has been made in developing therapeutics against Ebola Zaire, the species responsible for the 2014-

15 outbreak in West Africa. However those drugs may not be effective against Ebola Sudan. "That's why this latest study could be instrumental in reducing Ebola outbreaks," Geisbert said.

Since 2010, Ebola Sudan has been responsible for three outbreaks and until 2014, caused the largest outbreak of Ebola hemorrhagic fever on record, with 425 confirmed cases in Uganda in 2000.

"We were able to protect all of our nonhuman primates against a lethal Ebola Sudan infection when treatment began four days following infection," Geisbert said. "At this point, those infected showed signs of disease and had detectable levels of the virus in their blood."

Although all infected animals showed evidence of serious disease, those receiving the treatment survived and recovered. The untreated controls succumbed to the disease 8-10 days after exposure and had a disease course similar to that reported for Ebola Sudan-infected patients during outbreaks.

The treatment uses a specific short strand of RNA, known as siRNA, designed to target and interfere with the Ebola Sudan virus, rendering it harmless. One of the advantages of this approach is the ability to modify it to different viral species or strains. The siRNAs are delicate, so the researchers encapsulated them using a proprietary lipid nanoparticle (LNP) delivery technology platform developed by Arbutus Biopharma to protect the siRNAs in the bloodstream and allow efficient delivery and cellular uptake by the target cells. This clinically validated technology has been used successfully to protect non-human primates against Ebola Zaire and Marburg virus infection.

"Demonstrating protection in this uniformly lethal model of Ebola Sudan sets a high bar for determining effectiveness, as subjects were infected with a high viral dose that mimics the worst-case scenario of a needle-stick injury with concentrated viral material," said Geisbert. "The survival benefit and rapid control of viral replication with this treatment illustrate the strong potential of this evolving technology platform in combatting lethal viral infections."

Other authors include UTMB's Joan Geisbert, Krystle Agans, Daniel Deer, Karla Fenton and Chad Mire as well as Amy Lee and Emily Thi from Arbutus Biopharma Corporation in Vancouver, Canada.

The study was supported by the Centers of Excellence for Translational Research, which is an award of up to $26 million over a five-year period from the National Institute of Allergy and Infectious Diseases for a multi-project grant to advance the treatments of Ebola and Marburg virus infections.

http://bit.ly/2c689m8

Hope for reversing stroke-induced long-term disability

A human protein combined with stem cell therapy has been found to repair stroke damage to the brain, according to a new USC-led study on mice

Permanent brain damage from a stroke may be reversible thanks to a developing therapeutic technique, a USC-led study has found.

The novel approach combines transplanted human stem cells with a special protein that the U.S. Food and Drug Administration already approved for clinical studies in new stroke patients.

"This USC-led animal study could pave the way for a potential breakthrough in how we treat people who have experienced a stroke," said Jim Koenig, a program director at the National Institute of Neurological Disorders and Stroke, which funded the research. "If the therapy works in humans, it could markedly accelerate the recovery of these patients."

Berislav Zlokovic, senior author of the Aug. 22 Nature Medicine study, and his colleagues identified a protein that spurs neural stem cells to become functional neurons: 3K3A-APC, a variant of the human protein "activated protein C."

The created compound is being tested as a neuroprotectant. Researchers in a National Institutes of Health-funded Phase II clinical trial administer 3K3A-APC to patients who have very recently (within a few hours) suffered from an ischemic stroke, when a clot blocks blood from reaching the brain. About 87 percent of all strokes are ischemic, according to the Centers for Disease Control and Prevention.

However, Zlokovic, director of the Zilkha Neurogenetic Institute at the Keck School of Medicine of USC, said he and his colleagues are

the first to use 3K3A-APC to produce neurons from human stem cells grafted into the stroke-damaged mouse brain.

"We showed that 3K3A-APC helps the grafted stem cells convert into neurons and make structural and functional connections with the host's nervous system," said Zlokovic, a scientific founder of ZZ Biotech, a company devoted to developing therapeutics using variants of activated protein C. "No one in the stroke field has ever shown this, so I believe this is going to be the gold standard for future studies."

Although other researchers have experimented with grafting stem cells into injured brain areas, they have met with limited success -- partially because transplanted stem cells diminish with time. The therapeutic compound stops that from happening.

Every year more than 795,000 people in the United States have a stroke, according to the CDC. These debilitating seizures reduce mobility in more than half of stroke survivors age 65 and older.

More than 70 percent of stroke survivors live with substantial neurological symptoms such as muscle weakness or paralysis, according to Yaoming Wang, co-lead author of the study and a senior research associate at the Zilkha Neurogenetic Institute at the Keck School.

"The need for an efficacious, practical and late treatment of stroke remains unmet," Wang said. "Regenerative medicine with stem cells holds great promise for the treatment of stroke."

How combination therapy works

A week -- the equivalent of several months in humans -- after scientists induced a stroke in mice, the researchers placed human neural stem cells next to damaged brain tissue. Then they administered the immunosuppressant cyclosporine and four doses of 3K3A-APC or a placebo solution over a span of seven days.

The transplanted stem cells matured into neurons and other brain cells. Mice treated with the special compound had 16 times more human stem cell-derived neurons than those who were treated with the placebo.

"Functional deficit after five weeks of stroke were minimized, and the mice were almost back to normal in terms of motor and sensorimotor functions," Zlokovic said. "Synapses formed between transplanted cells and host cells, so there is functional activation and cooperation of transplanted cells in the host circuitry."

To test whether the injected stem cells caused the observed motor and sensorimotor improvements, USC researchers used an assassin toxin to exterminate neurons that developed from human stem cells. They found that these mice lost improvements in motor or sensory tests, suggesting the neurons that grew from implanted stem cells were necessary for recovery from stroke-induced disability.

The motor and sensory tests

Researchers tested motor functions by having mice walk forward on a rotating rod without falling off. They tested sensory and motor function by placing tape on the mouse's forepaw and observed how long it took the mice to remove the adhesive.

Rodents given human stem cells and treated with 3K3A-APC performed much better on these performance tests, said Zhen Zhao, co-lead author and an assistant professor of research physiology and biophysics at the Zilkha Neurogenetic Institute.

Functional integration

To test the brain's circuitry after the stroke, researchers labeled stem cells with an indicator of neuronal activity and then stimulated the paws of the mice with a mechanical vibration. They noted the injured area in 3K3A-APC-treated mice was activated much more than in mice treated with the placebo. Moreover, the response time was much closer to that of uninjured mice.

These results suggest that neurons which grew from the stem cells are functionally integrated into the host's brain circuitry.

The future of stem cell therapy

In June, Stanford University researchers drilled a hole into the skulls of people whose motor and sensory abilities had been compromised because of stroke. Then they injected stem cells harvested from the

bone marrow of adult donors. Although the study involved only 18 patients, researchers noted meaningful recovery, such as the ability to walk again. Stanford researchers said the stem cells seemed to trigger a biochemical process that enhanced the brain's ability to regenerate neurons. The transplanted stem cells themselves did not become neurons.

In contrast, researchers in the USC-led study were able to stimulate transplanted stem cells to becoming neurons in a mouse study.

Zlokovic and his team now hope to pursue a new Phase II clinical trial to test whether their combination therapy that stimulated the growth of neurons in mice can be replicated in human stroke patients. If the trial succeeds, they plan to extend the neural stem cell grafts and 3K3A-APC treatment to other neurological conditions, such as spinal cord injuries.

The study was supported by the National Institutes of Health, National Natural Science Foundation of China, Adelson Medical Research Foundation, New York State Stem Cell Research Board, Novo Nordisk Foundation, Lundbeck Foundation, National Multiple Sclerosis Society and the ALS Association.

http://bit.ly/2bNjlQv

Rx associated with fracture risk infrequently reduced after fracture occurrence

Is the occurrence of a fragility fracture - where Medicare beneficiaries broke a hip, wrist or shoulder - a missed opportunity to reduce exposure to prescription drugs associated with fracture risk?

Jeffrey C. Munson, M.D., M.S.C.E., of the Geisel School of Medicine at Dartmouth, Lebanon, N.H., and coauthors tried to answer that question in an article published online by JAMA Internal Medicine.

The authors analyzed data from a sample of Medicare beneficiaries because fragility fractures in older adults are a substantial source of sickness, death and health care costs. Patients who experience a fragility fracture are at increased risk of experiencing another one.

The study included 168,133 community-dwelling Medicare beneficiaries (84.2 percent of whom were women) who had an average age of 80 and who had survived a fracture of the hip, shoulder or wrist. Medicare Part D retail pharmacy claims were used to measure fills for prescriptions associated with increased fracture risk. There were 21 drugs classes divided into three categories: increased risk of fall, decreased bone density or unclear primary mechanism for increasing fracture risk.

The authors report:

About three-quarters of patients were using at least one nonopiate drug associated with increased fracture risk in the four months before their fracture.

About 7 percent of patients discontinued this drug after their fracture but that decrease was offset by new users of the drugs so the proportion did not change.

Limitations of the study include data that only included Part D enrollees who tend to have more coexisting illnesses and higher overall drug utilization rates so the results may not be generalizable to other groups.

The authors also note other caveats: many drugs have important indications that may preclude them from being discontinued after a fracture; the magnitude of the risk associated with many prescription drugs remains uncertain among those who survive fractures; and the way to improve physician prescribing practices after a fracture is not clearly developed.

"The use of drugs that can contribute to elevated fracture risk is common among Medicare beneficiaries who experience a fragility fracture, and the fracture event does not consistently lead to a reduction in use of these drugs. This suggests that at least some secondary fragility fractures may be preventable through a more concerted effort to manage high-risk drugs around a primary fracture event. Additional research is needed to quantify the possible benefits associated with modifying postfracture drug exposure in this high-risk population," the study concludes.

(JAMA Intern Med. Published online August 22, 2016.doi:10.1001/jamainternmed.2016.4814. Available pre-embargo to the media at http://media.jamanetwork.com.)

Editor's Note: Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Commentary: Medication Review After a Fracture - Absolutely Essential

"The findings of Munson et al suggest that far too often clinicians fail to perform a thoughtful medication review for patients with a fracture or to act on this review. A thoughtful review should include discussion of reducing or eliminating medications associated with falls and bone loss whenever possible," write Sherry D. Berry, M.D., M.P.H., and Douglas P. Kiel, M.D., M.P.H., of Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, in a related commentary.

http://bit.ly/2bOG9jN

New discovery in genetic research could lead to treatments for mitochondrial diseases

Embryos created with the presence of both maternal and paternal mitochondrial DNA

COLUMBIA, Mo. - A new study published in the Proceedings of the National Academy of Sciences (PNAS) from the University of Missouri has succeeded in creating embryos with "heteroplasmy," or the presence of both maternal and paternal mitochondrial DNA.

This new innovation will allow scientists to study treatments for mitochondrial diseases in humans as well as the significance of mitochondrial inheritance for livestock.

When parents pass along their genes to their children, most of the DNA from the mother and father is evenly divided.

However, children only receive one type of DNA, called mitochondrial DNA, from their mothers, while the fathers' mitochondrial DNA is naturally removed from the embryos.

Peter Sutovsky, a professor of reproductive physiology at Mizzou and lead author Won-Hee Song, a doctoral candidate in the Mizzou College of Agriculture, Food and Natural Resources, have found a way to prevent this paternal mitochondrial DNA removal process in pig embryos, thus creating embryos with "heteroplasmy."

"As many as 4,000 children are born in the U.S. every year with some form of mitochondrial disease, which can include poor growth, loss of muscle coordination, learning disabilities and heart disease," Sutovsky said.

"Some scientists believe some of these diseases may be caused by heteroplasmy, or cells possessing both maternal and paternal mitochondrial DNA. We have succeeded in creating this condition of heteroplasmy within pig embryos, which will allow scientists to further study whether paternal heteroplasmy could cause mitochondrial diseases in humans."

For their study, Sutovsky and Song identified two separate ubiquitin-binding proteins, called SQSTM1 and valosin-containing proteins (VCP), within embryos they believed were responsible for removing paternal, sperm-contributed mitochondria and their genetic cargo.

Sutovsky, Song and their colleagues experimented by inhibiting SQSTM1 and VCP separately, but found that even when one protein was incapacitated, the other protein still carried out the duty of disposing of the paternal mitochondria inside the fertilized egg. However, when Song and Sutovsky inhibited both proteins simultaneously, the paternal mitochondria were not removed and remained within the embryos.

"This research is important because we now know for sure what processes lead to the deletion of paternal mitochondrial DNA from embryos," Sutovsky said.

"This knowledge will enable us to further explore how some children may develop devastating mitochondrial diseases. From there, we can create treatments and therapies that may help prevent or reduce the effects of heteroplasmy and other mitochondrial disorders."

The study, "Autophagy and ubiquitin-proteasome system contribute to sperm mitophagy after mammalian fertilization," was funded by the National Institute of Food and Agriculture within the U.S. Department of Agriculture. Additional funding was provided by the National Institutes of Health Office of Research Infrastructure Programs, and by the Food for the 21st Century program at the University of Missouri. Stuart Meyers, a professor in the UC-Davis School of Veterinary Medicine, was a co-author on this study.

http://bit.ly/2beWQbp

NIH researchers discover otulipenia, a new inflammatory disease

Rare and sometimes lethal disease affects young children

National Institutes of Health researchers have discovered a rare and sometimes lethal inflammatory disease - otulipenia - that primarily affects young children. They have also identified anti-inflammatory treatments that ease some of the patients' symptoms: fever, skin rashes, diarrhea, joint pain and overall failure to grow or thrive.

Otulipenia is caused by the malfunction of OTULIN, a single gene on chromosome 5. When functioning properly, OTULIN regulates the development of new blood vessels and mobilization of cells and proteins to fight infection. NIH researchers published their findings Aug. 22, 2016, in the early edition of the Proceedings of the National Academy of Sciences.

Contributing to the work were researchers from the National Human Genome Research Institute (NHGRI), the National Institute of Allergy and Infectious Diseases, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Heart, Lung, and Blood Institute and the NIH Clinical Center, all part of NIH, along with their colleagues in Turkey and the United Kingdom.

"The results have been amazing and life changing for these children and their families," said Daniel Kastner, M.D., Ph.D., co-author, NHGRI scientific director and head of NHGRI's Inflammatory Disease Section. "We have achieved the important goal of helping these young patients and made progress in understanding the biological pathways and proteins that are important for the regulation of the immune system's responses." Cells use biological pathways to send and receive chemical cues in reaction to injury, infection or stress.

Otulipenia is one of several inflammatory diseases that occur when the immune system attacks the host's own tissues. Inflammation is the body's natural response to invading bacteria or viruses. The body releases chemicals that cause blood vessels to leak and tissues to swell in order to isolate a foreign substance from further contact with the body's tissues. Inflammatory diseases affecting the whole body are caused by mutations in genes like OTULIN that are part of a person's innate immunity (the cells and proteins present at birth that fight infections).

An international network of scientists studying inflammatory diseases identified four children from Pakistani and Turkish families with unexplained skin rashes and inflamed joints. NIH scientists then searched for disease-causing genes using next-generation DNA sequencing, technology that allows researchers to sequence DNA quickly and economically.

Once they found that the OTULIN gene was abnormal in the sick children, they studied the immune pathway in order to understand the mechanisms of disease and to improve treatment of these patients. They discovered a problem in the processing of a small protein, ubiquitin, which is critical to the regulation of many other proteins in the body, including immune molecules. In the affected children, the inability to remove the ubiquitin proteins from various molecules resulted in an increased production of chemical messengers that lead to inflammation (inflammatory cytokines).

The researchers determined that the children with otulipenia might respond to drugs that turned off tumor necrosis factor, a chemical messenger involved in systemic inflammation. Inflammation subsided in the children who had been treated with anti-tumor necrosis factor drugs (TNF inhibitors). TNF inhibitors are also used to treat chronic inflammatory diseases such as rheumatoid arthritis.

"The malfunction in this protein has not been previously linked to clinical disorders of the human immune system," said Ivona Aksentijevich, M.D., staff scientist in NHGRI's Medical Genetics Branch and study co-author. "This discovery suggests a direction that can be explored for development of new therapies for patients with a wide range of inflammatory diseases."

This study together with NIH's 2016 identification of haploinsufficiency of A20 (HA20), suggests a new category of human inflammatory diseases caused by impaired ubiquitination, according to the researchers.

NHGRI is one of the 27 institutes and centers at the NIH, an agency of the Department of Health and Human Services. The NHGRI Division of Intramural Research develops and implements technology to understand, diagnose and treat genomic and genetic diseases. Additional information about NHGRI can be found at: http://www.genome.gov.

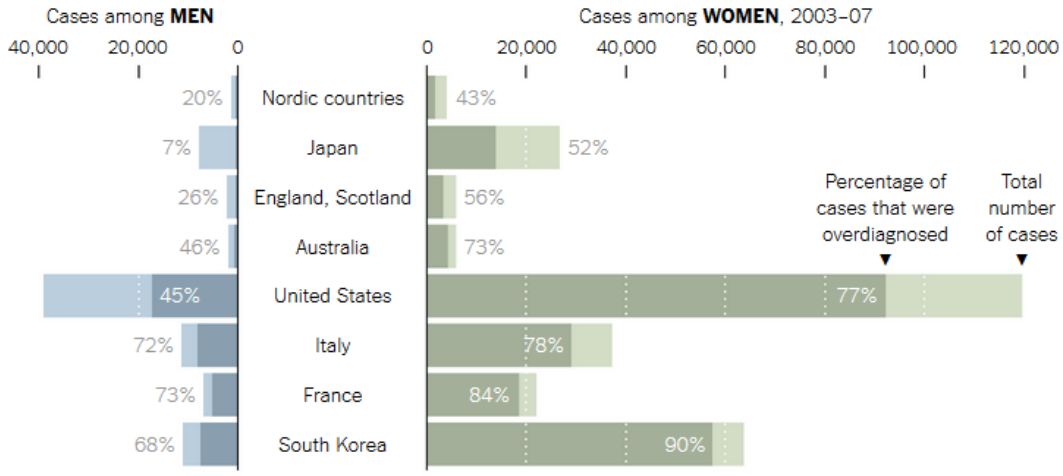
http://nyti.ms/2bVliNC

Got a Thyroid Tumor? Most Should Be Left Alone.

Up to 80 % of women told they had thyroid cancer often had their thyroids removed, but had tumors that should have been left alone

By GINA KOLATA AUG. 22, 2016

The data in a new report on thyroid cancer was stunning. From 2003 to 2007, as many as 70 percent to 80 percent of women in the United States, France, Italy and Australia who were told they had thyroid cancer and who often had their thyroids removed actually had tumors that should have been left alone.



Overdiagnosing Thyroid Cancer

Ultrasound and other scans may reveal small thyroid tumors, many of which would never progress if left alone. Aggressive treatment to remove the thyroid has lifelong consequences and has not reduced the death rate, a sign that thyroid cancer is being overdiagnosed.

Source: New England Journal of Medicine

By The New York Times

In South Korea, the trend is more pronounced — 90 percent of women with thyroid cancer probably did not require surgery.

The same trend applied to men, but to a lesser degree. In the United States and Australia, overdiagnosis accounted for about 45 percent of thyroid cancer in men over that four-year period. The rate in France, Italy and South Korea was about 70 percent, the report concluded.

The report in The New England Journal of Medicine by the International Agency for Research on Cancer in Lyon, France, and the Aviano National Cancer Institute in Aviano, Italy, though, was not a complete surprise to cancer researchers. Call it the downside of screening, or the law of unintended consequences. Or, as a reader suggested by email, “vomit,” for victim of modern imaging technology.

The increased use of scanning — ultrasound, CT, magnetic resonance imaging — is finding lumps in the neck that are too small to feel by hand. In South Korea, a national cancer screening program led doctors to actively look for such minuscule lumps by screening healthy people with ultrasound.

The result has been overdiagnosis. It happens with all cancer screening, but has been most apparent with thyroid cancer. And treatment is not benign.

Once doctors find a tiny nodule, removing the thyroid is often the remedy. But the procedure carries lifelong consequences: Patients must take thyroid hormones for the rest of their lives, and for some, those hormones are not completely effective. Patients can feel depressed and sluggish because their levels are too low.

Yet pathologists have long known that thyroid cancers, especially tiny ones, may never progress. Autopsies have shown that a third of people had them but never noticed them. The American Thyroid Association recently advised that when tiny tumors are discovered, the best course is watchful waiting — to leave the thyroid alone.

Some thyroid cancers, of course, really are dangerous, but they tend to be larger than the tiny ones found with scans. And symptoms like a lump in the neck or hoarseness should not be ignored.

The trend that has cancer experts wringing their hands began with ultrasound screens. They started coming into widespread use in the late 1980s. Gynecology and obstetrics clinics started screening healthy young women as part of routine examinations and finding little lumps. In addition, thyroid lumps were found accidentally when people had scans for other reasons. As ultrasound, M.R.I. and CT scans were used more and more, the thyroid cancer rate soared. In the United States, it has more than doubled since 1994. As many as 228,000 American women received thyroid cancer diagnoses from 1988 to 2007 as a result of overdiagnosis, according to the new report.

How would we know if there's an overdiagnosis problem? Simple, medical experts say. In a real cancer epidemic, deaths would increase in lock step with increasing incidence. But a rise in cancer cases while the death rate does not budge points to overdiagnosis.

And that, sadly enough, is what has happened.

http://bbc.in/2bVoVmK

Could mouthwash combat gonorrhoea?

"A gargle a day keeps gonorrhoea away" is an unlikely slogan, but researchers believe it could hold some truth.

By Michelle Roberts Health editor, BBC News online

Recent studies have shown people can carry the sexually transmitted infection in their throats for weeks or months without symptoms.

And they could spread it to others through unprotected oral sex.

So investigators are looking at whether regular mouthwash might help stop the silent spread and experts think it is an idea that is worth exploring.

The 'clap'

Gonorrhoea is a bacterium and it can live in secretions in the throat as well as the penis and vagina and is spread by oral, anal and vaginal sex. The disease - which was common in the first half of the 1900s until the discovery of an effective antibiotic treatment - is seeing a resurgence.

Doctors are worried that the number of new cases have been rocketing in recent years. Latest figures from Public Health England show that between 2012 and 2015 gonorrhoea infections rose by 53%, from 26,880 to 41,193. Medics are increasingly concerned that the infection may eventually become untreatable, following the emergence of "super-gonorrhoea" - a drug-resistant strain that can dodge the usual antibiotic used to treat it.

Super gonorrhoea

Public Health England recently detected an outbreak of azithromycin-resistant gonorrhoea in northern England.

Fortunately, the strain can still be treated with another antibiotic called ceftriaxone, but PHE says there's no room for complacency and it's monitoring the situation carefully.

If azithromycin becomes ineffective against gonorrhoea, there is no "second lock" to prevent or delay the emergence of ceftriaxone resistance and gonorrhoea may become untreatable, they warn.

Cases were first spotted in Leeds in November 2014. It then spread to the West Midlands and the south of England, with five cases found in London. By April 2016, the total number of people identified with the infection had reached 34 and included heterosexual couples and men who have sex with men.

Condoms are the best way to stop gonorrhoea spreading, but some experts believe there may also be another opportunity - mouthwash.

Studies suggests the throat could be a breeding ground for hard-to-treat bacteria. Gonorrhoea can persist here without symptoms and swap DNA with other throat microbes that already know how to dodge certain antibiotics.

Prof Christopher Fairley from Monash University has been testing the mouthwash theory in 58 male volunteers. All of the men had detectable levels of throat gonorrhoea at the start of the trial.

He asked half of them to gargle and swill for a minute with saltwater while he gave the others a branded antiseptic mouthwash, bought from a supermarket, to use instead. He retested them five minutes later to see if the gargling had helped. It appeared to, reducing the detectable amount of bacteria significantly more than the saltwater rinse.

Prof Fairley says more studies are needed to check how long this effect might last and what protection it might offer.He's now recruiting more volunteers to take part in a three-month trial to see what impact daily gargling might have on gonorrhoea throat carriage.

Dr Anatole Menon-Johansson is an expert in sexual health and clinical director for the charity Brook.

He says Prof Fairley "could well be on to something".

"I heard his presentation at a medical conference and I was really impressed. It's obviously still only a hypothesis. There's lots more to do and explore. But it's interesting, and it's got everybody thinking.

"If you could use a mouthwash there's a chance at the population level that it might make a difference to infection rates."

Men visiting his sexual health clinic are offered pharyngeal testing for gonorrhoea. If the test comes back positive, the clinic runs extra checks to see what treatments the bacteria will respond to and which ones are doomed to fail because of drug resistance.

"These organisms have been with us humans for thousands of years and will continue to be. The challenge is working out ways to control transmission and make sure we have drugs that can still treat it."

Dr Gwenda Hughes, Head of the Sexually Transmitted Infections (STIs) Section at Public Health England (PHE), said: "Gonorrhoea infection in the throat usually has no symptoms but both men and women can get it by having unprotected oral sex.

"The only protection is by using condoms when having sex with new or casual partners and it's important to have regular check-ups at a sexual health clinic. Sexually active gay, bisexual or other men who have sex with men should get tested for STI's at least every three months.

"PHE continues to monitor, and act on, the spread of antibiotic resistance and potential gonorrhoea treatment failures by investigating identified cases, sexual history and treatment to make sure they are managed promptly."

Gonorrhoea

Gonorrhoea can affect anyone who has had unprotected sex

One in 10 men and half of women with gonorrhoea will have no signs or symptoms

Symptoms can include a yellow or green discharge and burning sensation when urinating

Doctors can test for gonorrhoea by sending off a swab or a urine sample

Previous successful treatment for gonorrhoea doesn't make you immune to catching the infection again

http://bit.ly/2bFLviX

Fossilized rivers suggest warm, wet ancient Mars

Extensive fossilised riverbeds on the Martian surface support the idea that the Red Planet was warm and wet about 4 billion years ago

Extensive systems of fossilised riverbeds have been discovered on an ancient region of the Martian surface, supporting the idea that the now cold and dry Red Planet had a warm and wet climate about 4 billion years ago, according to UCL-led research.

The study, published in Geology and funded by the Science & Technology Facilities Council and the UK Space Agency, identified over 17,000km of former river channels on a northern plain called Arabia Terra, providing further evidence of water once flowing on Mars.

"Climate models of early Mars predict rain in Arabia Terra and until now there was little geological evidence on the surface to support this theory. This led some to believe that Mars was never warm and wet but was a largely frozen planet, covered in ice-sheets and glaciers. We've now found evidence of extensive river systems in the area which supports the idea that Mars was warm and wet, providing a

more favourable environment for life than a cold, dry planet," explained lead author, Joel Davis (UCL Earth Sciences).

Since the 1970s, scientists have identified valleys and channels on Mars which they think were carved out and eroded by rain and surface runoff, just like on Earth. Similar structures had not been seen on Arabia Terra until the team analysed high resolution imagery from NASA's Mars Reconnaissance Orbiter (MRO) spacecraft.

The new study examined images covering an area roughly the size of Brazil at a much higher resolution than was previously possible - 6 metres per pixel compared to 100 metres per pixel. While a few valleys were identified, the team revealed the existence of many systems of fossilised riverbeds which are visible as inverted channels spread across the Arabia Terra plain.

The inverted channels are similar to those found elsewhere on Mars and Earth. They are made of sand and gravel deposited by a river and when the river becomes dry, the channels are left upstanding as the surrounding material erodes. On Earth, inverted channels often occur in dry, desert environments like Oman, Egypt, or Utah, where erosion rates are low - in most other environments, the channels are worn away before they can become inverted.

"The networks of inverted channels in Arabia Terra are about 30m high and up to 1-2km wide, so we think they are probably the remains of giant rivers that flowed billions of years ago. Arabia Terra was essentially one massive flood plain bordering the highlands and lowlands of Mars. We think the rivers were active 3.9-3.7 billion years ago, but gradually dried up before being rapidly buried and protected for billions of years, potentially preserving any ancient biological material that might have been present," added Joel Davis.

"These ancient Martian flood plains would be great places to explore to search for evidence of past life. In fact, one of these inverted channels called Aram Dorsum is a candidate landing site for the European Space Agency's ExoMars Rover mission, which will launch in 2020," said Dr Matthew Balme, Senior Lecturer at The Open University and co-author of the study.

The researchers now plan on studying the inverted channels in greater detail, using higher-resolution data from MRO's HiRISE camera.

http://www.bbc.com/news/health-37166293

Depression: A revolution in treatment?

It's not very often we get to talk about a revolution in understanding and treating depression and yet now doctors are talking about "one of the strongest discoveries in psychiatry for the last 20 years".

By James Gallagher, Rachael Buchanan & Andrew Luck-Baker The Inflamed Mind, BBC Radio 4

It is based around the idea that some people are being betrayed by their fiercest protector. That their immune system is altering their brain.

The illness exacts a heavy toll on 350 million people around the world, among them Hayley Mason, from Cambridgeshire: "My depression gets so bad that I can't leave the bed, I can't leave the bedroom, I can't go downstairs and be with my partner and his kids.

The 30-year-old added: "I can't have the TV on, I can't have noise and light, I have suicidal thoughts, I have self-harmed, I can't leave the house, I can't drive. "And just generally I am completely confined to my own home and everything else just feels too much."

Anti-depressant drugs and psychological treatments, like cognitive behavioural therapy, help the majority of people. But many don't respond to existing therapies and so some scientists are now exploring a new frontier - whether the immune system could be causing depression.

"I think we have to be quite radical," says Prof Ed Bullmore, the head of psychiatry at the University of Cambridge. He's at the forefront of this new approach: "Recent history is telling us if we want to make therapeutic breakthroughs in an area which remains incredibly important in terms of disability and suffering then we've got to think differently."

The focus is on an errant immune system causing inflammation in the body and altering mood.

And Prof Bullmore argues that's something we can all relate to, if we just think back to the last time we had a cold or flu. He said: "Depression and inflammation often go hand in hand, if you have flu, the immune system reacts to that, you become inflamed and very often people find that their mood changes too. "Their behaviour changes, they may become less sociable, more sleepy, more withdrawn.

"They may begin to have some of the negative ways of thinking that are characteristic of depression and all of that follows an infection."

It is a subtle and yet significant shift in thinking. The argument is we don't just feel sorry for ourselves when we are sick, but that the chemicals involved in inflammation are directly affecting our mood.

Inflammation is part of the immune system's response to danger. It is a hugely complicated process to prepare our body to fight off hostile forces. If inflammation is too low then an infection can get out of hand. If it is too high, it causes damage.

And for some reason, about one-third of depressed patients have consistently high levels of inflammation. Hayley is one of them: "I do have raised inflammation markers, I think normal is under 0.7 and mine is 40, it's coming up regularly in blood tests."

There is now a patchwork quilt of evidence suggesting inflammation is more than something you simply find in some depressed patients, but is actually the cause of their disease. That the immune system can alter the workings of the brain.

Joint pain

To explore this revolutionary new idea in depression, we visited an arthritis clinic at Glasgow Royal Infirmary. It is perhaps an unexpected location, but it was in clinics like this that doctors noticed something unusual. Rheumatoid arthritis is caused by the immune system attacking the joints. And when patients were given precise anti-inflammatory drugs that calmed down specific parts of the immune response, their mood improved.

Prof Iain McInnes, a consultant rheumatologist, said: "When we give these therapies we see a fairly rapid increase in a sense of well-being, mood state improving quite remarkably often disproportionately given the amount of inflammation we can see in their joints and their skin."

It suggests the patients were not simply feeling happier as they were in less pain, but that something more profound was going on.

Prof McInnes added: "We scanned the brains of people with rheumatoid arthritis, we then gave them a very specific immune targeted therapy and then we imaged them again afterwards. "What we are starting to see when we give anti-inflammatory medicines is quite remarkable changes in the neuro-chemical circuitry in the brain."The brain pathways involved in mediating depression were favourably changed in people who were given immune interventions."

One possible explanation is that inflammatory chemicals enter the brain. There they interrupt the production of serotonin - a key neurotransmitter that's linked to mood.

To hear more we visited Carmine Pariante's laboratory at King's College London. The professor of biological psychiatry has been piecing together the evidence on inflammation and depression for 20 years. He told the BBC: "Nearly 30% to 40% of depressed patients have high levels of inflammation and in these people we think it is part of the causal process. "The evidence supporting this idea is that high levels of inflammation are present even if someone is not depressed, but is at risk of becoming depressed.

"We know from studies that if you have high levels of inflammation today you're at higher risk of becoming depressed over the next weeks or months even if you are perfectly well."

He's shown that not only are depressed patients more likely to have high levels of inflammation, but those with an overactive immune system are also less likely to respond to anti-depressants. This is a big deal because a third of patients don't get any benefit from drug treatments. But there's something confusing here. The immune system

responds to infection and that doesn't seem to fit the usual story of depression.

Take Jennifer Streeting, a trainee midwife in London, who traces her mental health problems back to when she was 14. "My nana passed away and my mum had breast cancer and if you ask my therapist now she puts it down to grief and not really dealing with that at the time, I think there was just a lot going on."

Prof Pariante argues it is actually these awful moments in our lives that change our immune system, priming it to increase the risk of depression years later. He said: "We think the immune system is the key mechanism by which early life events produce this long-term effect. "We have some data showing adult individuals who have a history of early life trauma, even if they have never been depressed, have an activated immune system so they are in a state of risk."

The hope is that drugs targeting the immune system will provide much needed treatments for patients, particularly for those like Jennifer who seem to have tried them all.

"I had sertraline, I had Prozac, there was another one, I got started on citalopram, I was put on duloxetine, mirtazapine as well. I was on three at one point." She is now on a combination of drugs that seem to be working for her, but it has been a long journey.

"It is totally trial and error," said Prof Pariante. He added: "We are not able to predict right from the beginning whether someone will respond. "We think by measuring inflammation in the blood we'll actually be able to identify individuals that do require more complex, intensive antidepressant treatment, maybe a combination of an antidepressant and and anti-inflammatory."

Most of us have common anti-inflammatories like ibuprofen at home, but doctors warn against experimenting at home, while clinical trials are taking place to prove whether this will work in patients.

The world's largest medical research charity, the Wellcome Trust, has brought together universities and the pharmaceutical industry.

The aim is to consolidate the evidence to accelerate the field; ultimately they want to find a new treatment for depression and develop a test to identify those who will benefit.

Cambridge University's Prof Bullmore is leading the consortium. But we interviewed him at his other employer, GlaxoSmithKline.

The company's immuno-inflammation laboratory is where scientists are developing new molecules which they hope will become effective medicines for inflammatory disorders.

That process will take more than a decade, but Prof Bullmore says there may already be a drug out there.

"One of the exciting things about immunopsychiatry is that because of the success of immunology in other areas of medicine there are already many drugs that are far beyond this stage of development.

"They may already be licensed or in late-stage clinical trials so the timeline from start of work on that project to delivering a medicine that might make a difference to patients could be much shorter."

Progress

Raiding the cupboards is already showing signs of success. Those early clues in arthritis mean the anti-inflammatory drug sirukumab is now being trialled in depressed patients. So are drugs targeting the immune system about to transform the treatment of depression?

Prof Bullmore argues: "I don't think they are going to be a panacea, I don't think we're talking about a scenario in future where every patient with symptoms of depression is going to be offered an anti-inflammatory drug. "I don't think that makes sense and frankly that sort of blockbuster one-size-fits-all approach to development of drugs for psychiatry has not been helpful to us in the past.

"We have to take a more personalised or stratified approach, not everyone that is depressed is depressed for the same reason."

That will require a blood test to identify which patients will benefit from immune-based therapies.

Depression is a disease that affects hundreds of millions of people. Even if anti-inflammatories help just a small proportion of them - that

would still be a huge number of patients. But if immunotherapy becomes a success, its biggest impact may be on the way we think about the disease, making people less likely to believe sufferers should just "pull themselves together".

"I hate that phrase, if I could I would," says Jennifer. She adds: "Just as if someone had diabetes and their insulin levels weren't working correctly, you wouldn't say, 'Oh snap out of it, stop having a hypo.'"

Hayley feels the same: "If there was a way to say depression was a physical problem I think it would make a massive difference, I think people would treat depression as something that is not made up and going on in the head. "It would be seen as a genuine condition, it would validate a lot of people's feelings."

Prof Pariante concludes: "It is groundbreaking because, for the first time, we are demonstrating that depression is not only a disorder of the mind, in fact it is not even only a disorder of the brain, it is a disorder of the whole body."

http://wb.md/2boTRco

The More RNs, the Higher the Patient Survival

Staff Ratios and Mortality

Margaret R. Nolan, DNP, GNP

Many studies have been done looking at the association between lower numbers of registered nurses (RNs) and increased patient mortality. Survival rates for patients who experience cardiac events can vary as much as 42% among different hospitals with similar patient populations.[1] A new study by McHugh and colleagues[2] examines patient survival rates after cardiac arrest in the context of the work environment and RN staffing ratios.

The investigators directly surveyed bedside nurses using the 31-item Practice Environment Scale of the Nurses Work Index. They found that each additional patient per nurse on a medical-surgical unit was associated with a 5% lower odds of survival and a 16% lower odds of survival for patients in hospitals with poor work environments (both findings were statistically significant.) The conclusion from this study is that better hospital work environments and adequate hospital RN staffing are important strategies in improving patient survival rates.

Viewpoint

The relationship between RN staffing and patient outcomes is modified by the characteristics of the working environment. This suggests that merely adding more nurses without improving the environment may not be enough to have an impact on patient survival. Improving the environment involves giving RNs more autonomy, control over practice, resources, and good working relationships and communication with physicians. This study adds to the growing evidence that better RN staffing and work environments can improve patient survival.

An important article, published in the *New England Journal of Medicine*[3] in 2011, found that below-target RN staffing patterns and high patient turnover increased the risk for patient death. New healthcare financing reforms are designed to reward accountability and efficiency, and to bundle services and costs. The cost of RN staffing must also be taken into account.[3]

Safe staffing has been part of the healthcare conversation for many decades. In 2004, California became the first state to establish minimum RN-to-patient ratios for hospitals. This bill, which was passed in 1999 and implemented in 2003, required California acute care hospitals to meet the new staffing ratios by 2004.[4]

The American Nurses Association (ANA) has supported a safe staffing plan that includes the following[5]:

- ***Establish a minimum number of RNs that is adjustable;***
- ***Solicit input from direct care RNs; staff RNs should be represented on staffing committees;***
- ***Base RN staffing on census and patient acuity levels;***
- ***Take into account the experience level of RNs;***
- ***Consider staffing recommendation from nursing specialty organizations; and***
- ***Ensure that RNs are not forced to float into areas where they have no experience.***

The ANA is concerned that legislating minimum RN staffing levels (nurse-to-patient ratios) can fail to account for unique factors, such as patient acuity, skill mix of the nurses, use of ancillary staff, and even architectural features of the work setting. The ANA is also concerned that legislated ratios lack flexibility, and will lead to a reduction in ancillary staffing to meet the RN staffing requirements.[3]

In New York State, where I practice, the state assembly passed the Safe Staffing for Quality Care Act on June 15, 2015.[6] Support for this safe staffing bill was generated by petitions and patients' rights groups, all citing studies that show an increase risk for patient death for each new patient assigned to a nurse. The legislature has included the establishment of safe patient workloads, using nurses trained specifically to the unit on which they work, making it necessary for hospitals to be forthcoming about their staffing patterns and setting a maximum of patients that any nurse can care for.[6] This bill now needs to pass in the state senate and be signed by the governor. The senate already showed support for the bill for safe staffing throughout New York State hospitals in January 2015.[7]

Studies show that Magnet facilities have higher nurse-to-patient ratios and professional practice environments that result in fewer complications, lower mortality rates, and shorter stays.[7] Hospitals applying for Magnet status can improve the work environment for their nurses. Magnet recognition by the American Nurses Credentialing Center requires a culture shift throughout a healthcare organization and takes a constant effort by hospitals to be maintained.[7] Staffing ratios play an important role in patient survival in the hospital, but good working environments prove to be just as important and will need to be addressed by hospitals and nursing leaders throughout the country if we are to have an impact on patient survival.

References

1. Merchant RM, Berg RA, Yang L, Becker LB, Groeneveld PW, Chan PS; American Heart Association's Get With the Guidelines-Resuscitation Investigators. Hospital variation in survival after in-hospital cardiac arrest. J Am Heart Assoc. 2014;3:e000400.

2. McHugh MD, Rochman MF, Sloane DM, et al; American Heart Association's Get With the Guidelines-Resuscitation Investigators. Better nurse staffing and nure work environments associated with increased survival of in-hospital cardiac arrest patients. Med Care. 2016;54:74-80. Abstract

3. Needleman J, Buerhaus P, Pankratz VS, Leibson CL, Stevens SR, Harris M. Nurse staffing and inpatient hospital mortality. N Engl J Med. 2011;364;1037-1045. Abstract

4. Kasprak J. California RN staffing ratio law. California Nurses Association. February 10, 2004. https://www.cga.ct.gov/2004/rpt/2004-R-0212.htm Accessed August 9, 2016.

5. American Nurses Association. Safe staffing. http://www.nursingworld.org/SafeStaffingFactsheet.aspx Accessed August 9, 2016.

6. Perez-Wallach A. Nurses unions, patient tights groups and lawmakers representing tens of thousands of New Yorkers call on the New York State senate to pass the Safe Staffing for Quality Care Act. Citizen Action of New York. June 15, 2016. http://citizenactionny.org/2016/06/nurses-unions-patient-rights-groups-lawmakers-representing-tens-thousands-new-yorkers-call-new-york-state-senate-pass-safe-staffing-quality-care-act/20645 Accessed August 9, 2016.

7. New York State Assembly. S01936 summary. http://assembly.state.ny.us/leg/?default_fld=&bn=S01936&Summary=Y&Actions=Y&Text=Y&Votes=Y Accessed August 9, 2016.

http://bit.ly/2bjHQTD

Humans have caused climate change for 180 years

An international research project has found human activity has been causing global warming for almost two centuries, proving human-induced climate change is not just a 20th century phenomenon.

Lead researcher Associate Professor Nerilie Abram from The Australian National University (ANU) said the study found warming began during the early stages of the Industrial Revolution and is first detectable in the Arctic and tropical oceans around the 1830s, much earlier than scientists had expected.

"It was an extraordinary finding," said Associate Professor Abram, from the ANU Research School of Earth Sciences and ARC Centre of Excellence for Climate System Science.

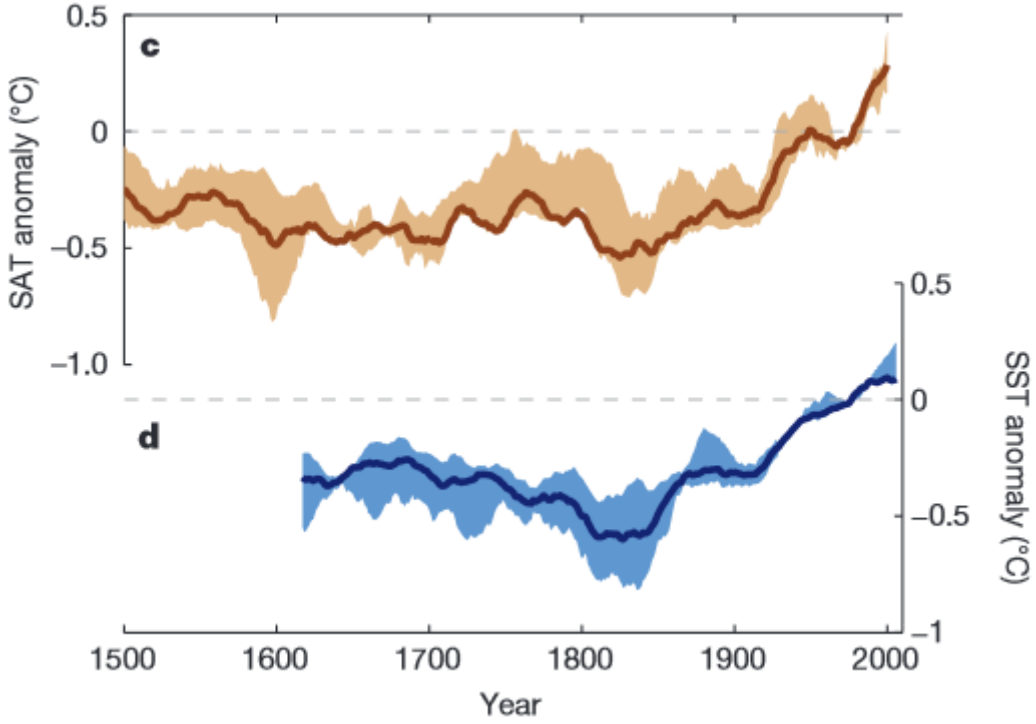
"It was one of those moments where science really surprised us. But the results were clear. The climate warming we are witnessing today started about 180 years ago."

The new findings have important implications for assessing the extent that humans have caused the climate to move away from its pre-

industrial state, and will help scientists understand the future impact of greenhouse gas emissions on the climate.

"In the tropical oceans and the Arctic in particular, 180 years of warming has already caused the average climate to emerge above the range of variability that was normal in the centuries prior to the Industrial Revolution," Associate Professor Abram said.

Figure 1 | Terrestrial and marine palaeoclimate reconstructions



c, d, 25-year moving averages of the area-weighted mean terrestrial temperature anomaly (brown line) 4, 16 and the 25%–75% range across continental-scale reconstructions (shading) (c) and area-weighted mean tropical SST anomaly (blue line) and minimum–maximum range across the Indian, western Pacific and western Atlantic reconstructions 14 (shading) (d). Anomalies are relative to the ad 1961–1990 mean (dashed lines).

The research, published in Nature, involved 25 scientists from across Australia, the United States, Europe and Asia, working together as part of the international Past Global Changes 2000 year (PAGES 2K) Consortium.

Associate Professor Abram said anthropogenic climate change was generally talked about as a 20th century phenomenon because direct measurements of climate are rare before the 1900s. However, the team studied detailed reconstructions of climate spanning the past 500 years to identify when the current sustained warming trend really began.

Scientists examined natural records of climate variations across the world's oceans and continents. These included climate histories preserved in corals, cave decorations, tree rings and ice cores.

The research team also analysed thousands of years of climate model simulations, including experiments used for the latest report by the UN's Intergovernmental Panel on Climate Change (IPCC), to determine what caused the early warming.

The data and simulations pinpointed the early onset of warming to around the 1830s, and found the early warming was attributed to rising greenhouse gas levels.

Co-researcher Dr Helen McGregor, from the University of Wollongong's School of Earth and Environmental Sciences, said humans only caused small increases in the level of greenhouse gases in the atmosphere during the 1800s. "But the early onset of warming detected in this study indicates the Earth's climate did respond in a rapid and measureable way to even the small increase in carbon emissions during the start of the Industrial Age," Dr McGregor said.

The researchers also studied major volcanic eruptions in the early 1800s and found they were only a minor factor in the early onset of climate warming.

Associate Professor Abram said the earliest signs of greenhouse-induced warming developed during the 1830s in the Arctic and in tropical oceans, followed soon after by Europe, Asia and North America. However, climate warming appears to have been delayed in the Antarctic, possibly due to the way ocean circulation is pushing warming waters to the North and away from the frozen continent.

A video, video news release, images, FAQ, and a copy of the research paper is available at https://cloudstor.aarnet.edu.au/plus/index.php/s/4pQheVzMddCXwJN.

http://bit.ly/2bBn56S

Planet found in habitable zone around nearest star

Pale Red Dot campaign reveals Earth-mass world in orbit around Proxima Centauri

Astronomers using ESO telescopes and other facilities have found clear evidence of a planet orbiting the closest star to Earth, Proxima Centauri. The long-sought world, designated Proxima b, orbits its cool red parent star every 11 days and has a temperature suitable for liquid water to exist on its surface. This rocky world is a little more massive than the Earth and is the closest exoplanet to us -- and it may also be the closest possible abode for life outside the Solar System. A paper describing this milestone finding will be published in the journal Nature on 25 August 2016.

Just over four light-years from the Solar System lies a red dwarf star that has been named Proxima Centauri as it is the closest star to Earth apart from the Sun. This cool star in the constellation of Centaurus is too faint to be seen with the unaided eye and lies near to the much brighter pair of stars known as Alpha Centauri AB.

During the first half of 2016 Proxima Centauri was regularly observed with the HARPS spectrograph on the ESO 3.6-metre telescope at La Silla in Chile and simultaneously monitored by other telescopes around the world [1]. This was the Pale Red Dot campaign, in which a team of astronomers led by Guillem Anglada-Escudé, from Queen Mary University of London, was looking for the tiny back and forth wobble of the star that would be caused by the gravitational pull of a possible orbiting planet [2].

As this was a topic with very wide public interest, the progress of the campaign between mid-January and April 2016 was shared publicly as it happened on the Pale Red Dot website and via social media. The reports were accompanied by numerous outreach articles written by specialists around the world.

Guillem Anglada-Escudé explains the background to this unique search: "The first hints of a possible planet were spotted back in 2013, but the detection was not convincing. Since then we have worked hard to get further observations off the ground with help from ESO and others. The recent Pale Red Dot campaign has been about two years in the planning."

The Pale Red Dot data, when combined with earlier observations made at ESO observatories and elsewhere, revealed the clear signal of a truly exciting result. At times Proxima Centauri is approaching Earth at about 5 kilometres per hour -- normal human walking pace -- and at times receding at the same speed. This regular pattern of changing radial velocities repeats with a period of 11.2 days. Careful analysis of the resulting tiny Doppler shifts showed that they indicated the presence of a planet with a mass at least 1.3 times that of the Earth, orbiting about 7 million kilometres from Proxima Centauri -- only 5% of the Earth-Sun distance [3].

Guillem Anglada-Escudé comments on the excitement of the last few months: "I kept checking the consistency of the signal every single day during the 60 nights of the Pale Red Dot campaign. The first 10 were promising, the first 20 were consistent with expectations, and at 30 days the result was pretty much definitive, so we started drafting the paper!"

Red dwarfs like Proxima Centauri are active stars and can vary in ways that would mimic the presence of a planet. To exclude this possibility the team also monitored the changing brightness of the star very carefully during the campaign using the ASH2 telescope at the San Pedro de Atacama Celestial Explorations Observatory in Chile and the Las Cumbres Observatory telescope network. Radial velocity data taken when the star was flaring were excluded from the final analysis.

Although Proxima b orbits much closer to its star than Mercury does to the Sun in the Solar System, the star itself is far fainter than the Sun. As a result Proxima b lies well within the habitable zone around the star and has an estimated surface temperature that would allow the presence of liquid water. Despite the temperate orbit of Proxima b, the

conditions on the surface may be strongly affected by the ultraviolet and X-ray flares from the star -- far more intense than the Earth experiences from the Sun [4].

Two separate papers discuss the habitability of Proxima b and its climate. They find that the existence of liquid water on the planet today cannot be ruled out and, in such case, it may be present over the surface of the planet only in the sunniest regions, either in an area in the hemisphere of the planet facing the star (synchronous rotation) or in a tropical belt (3:2 resonance rotation). Proxima b's rotation, the strong radiation from its star and the formation history of the planet makes its climate quite different from that of the Earth, and it is unlikely that Proxima b has seasons.

This discovery will be the beginning of extensive further observations, both with current instruments [5] and with the next generation of giant telescopes such as the European Extremely Large Telescope (E-ELT). Proxima b will be a prime target for the hunt for evidence of life elsewhere in the Universe. Indeed, the Alpha Centauri system is also the target of humankind's first attempt to travel to another star system, the StarShot project.

Guillem Anglada-Escudé concludes: "Many exoplanets have been found and many more will be found, but searching for the closest potential Earth-analogue and succeeding has been the experience of a lifetime for all of us. Many people's stories and efforts have converged on this discovery. The result is also a tribute to all of them. The search for life on Proxima b comes next..."

Notes

[1] Besides data from the recent Pale Red Dot campaign, the paper incorporates contributions from scientists who have been observing Proxima Centauri for many years. These include members of the original UVES/ESO M-dwarf programme (Martin Kürster and Michael Endl), and exoplanet search pioneers such as R. Paul Butler. Public observations from the HARPS/Geneva team obtained over many years were also included.

[2] The name Pale Red Dot reflects Carl Sagan's famous reference to the Earth as a pale blue dot. As Proxima Centauri is a red dwarf star it will bathe its orbiting planet in a pale red glow.

[3] The detection reported today has been technically possible for the last 10 years. In fact, signals with smaller amplitudes have been detected previously. However, stars are not smooth balls of gas and Proxima Centauri is an active star. The robust detection of Proxima b has only been possible after reaching a detailed understanding of how the star changes on timescales from minutes to a decade, and monitoring its brightness with photometric telescopes.

[4] The actual suitability of this kind of planet to support water and Earth-like life is a matter of intense but mostly theoretical debate. Major concerns that count against the presence of life are related to the closeness of the star. For example gravitational forces probably lock the same side of the planet in perpetual daylight, while the other side is in perpetual night. The planet's atmosphere might also slowly be evaporating or have more complex chemistry than Earth's due to stronger ultraviolet and X-ray radiation, especially during the first billion years of the star's life. However, none of the arguments has been proven conclusively and they are unlikely to be settled without direct observational evidence and characterisation of the planet's atmosphere. Similar factors apply to the planets recently found around TRAPPIST-1.

[5] Some methods to study a planet's atmosphere depend on it passing in front of its star and the starlight passing through the atmosphere on its way to Earth. Currently there is no evidence that Proxima b transits across the disc of its parent star, and the chances of this happening seem small, but further observations to check this possibility are in progress.

More information

This research is presented in a paper entitled "A terrestrial planet candidate in a temperate orbit around Proxima Centauri", by G. Anglada-Escudé et al., to appear in the journal Nature on 25 August 2016.

The team is composed of Guillem Anglada-Escudé (Queen Mary University of London, London, UK), Pedro J. Amado (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), John Barnes (Open University, Milton Keynes, UK), Zaira M. Berdiñas (Instituto de Astrofísica de Andalucia - CSIC, Granada, Spain), R. Paul Butler (Carnegie Institution of Washington, Department of Terrestrial Magnetism, Washington, USA), Gavin A. L. Coleman (Queen Mary University of London, London, UK), Ignacio de la Cueva (Astroimagen, Ibiza, Spain), Stefan Dreizler (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), Michael Endl (The University of Texas at Austin and McDonald Observatory, Austin, Texas, USA), Benjamin Giesers (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), Sandra V. Jeffers (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), James S. Jenkins (Universidad de Chile, Santiago, Chile), Hugh R. A. Jones (University of Hertfordshire, Hatfield, UK), Marcin Kiraga (Warsaw University Observatory, Warsaw, Poland), Martin Kürster (Max-Planck-Institut für Astronomie, Heidelberg, Germany), María J. López-González (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), Christopher J. Marvin (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), Nicolás Morales (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), Julien Morin (Laboratoire Univers et Particules de Montpellier, Université de Montpellier & CNRS, Montpellier, France), Richard P. Nelson (Queen Mary University of London, London, UK), José L. Ortiz (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), Aviv Ofir (Weizmann Institute of Science, Rehovot, Israel), Sijme-Jan Paardekooper (Queen Mary University of London, London, UK), Ansgar Reiners (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), Eloy Rodriguez (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), Cristina Rodriguez-Lopez (Instituto de Astrofísica de Andalucía - CSIC, Granada, Spain), Luis F. Sarmiento (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany), John P. Strachan (Queen Mary University of London, London, UK), Yiannis Tsapras (Astronomisches Rechen-Institut, Heidelberg, Germany), Mikko Tuomi (University of Hertfordshire, Hatfield, UK) and Mathias Zechmeister (Institut für Astrophysik, Georg-August-Universität Göttingen, Göttingen, Germany).

Research paper in Nature -
http://www.eso.org/public/archives/releases/sciencepapers/eso1629/eso1629a.pdf
Two new papers on Habitability on Proxima b - http://www.proximacentauri.info

http://bit.ly/2bXl20u

UCLA scientists use ultrasound to jump-start a man's brain after coma

New noninvasive technique may lead to low-cost therapy for patients with severe brain injury

A 25-year-old man recovering from a coma has made remarkable progress following a treatment at UCLA to jump-start his brain using ultrasound. The technique uses sonic stimulation to excite the neurons in the thalamus, an egg-shaped structure that serves as the brain's central hub for processing information.

"It's almost as if we were jump-starting the neurons back into function," said Martin Monti, the study's lead author and a UCLA associate professor of psychology and neurosurgery. "Until now, the only way to achieve this was a risky surgical procedure known as deep brain stimulation, in which electrodes are implanted directly inside the thalamus," he said. "Our approach directly targets the thalamus but is noninvasive."

Monti said the researchers expected the positive result, but he cautioned that the procedure requires further study on additional patients before they determine whether it could be used consistently to help other people recovering from comas. "It is possible that we were just very lucky and happened to have stimulated the patient just as he was spontaneously recovering," Monti said. A report on the treatment is published in the journal Brain Stimulation. This is the first time the approach has been used to treat severe brain injury.

The technique, called low-intensity focused ultrasound pulsation, was pioneered by Alexander Bystritsky, a UCLA professor of psychiatry and biobehavioral sciences in the Semel Institute for Neuroscience and Human Behavior and a co-author of the study. Bystritsky is also a founder of Brainsonix, a Sherman Oaks, California-based company that provided the device the researchers used in the study.

That device, about the size of a coffee cup saucer, creates a small sphere of acoustic energy that can be aimed at different regions of the brain to excite brain tissue. For the new study, researchers placed it by the side of the man's head and activated it 10 times for 30 seconds each, in a 10-minute period. Monti said the device is safe because it emits only a small amount of energy -- less than a conventional Doppler ultrasound.

Before the procedure began, the man showed only minimal signs of being conscious and of understanding speech -- for example, he could perform small, limited movements when asked. By the day after the treatment, his responses had improved measurably. Three days later, the patient had regained full consciousness and full language comprehension, and he could reliably communicate by nodding his head "yes" or shaking his head "no." He even made a fist-bump gesture to say goodbye to one of his doctors.

"The changes were remarkable," Monti said.

The technique targets the thalamus because, in people whose mental function is deeply impaired after a coma, thalamus performance is typically diminished. And medications that are commonly prescribed to people who are coming out of a coma target the thalamus only indirectly.

Under the direction of Paul Vespa, a UCLA professor of neurology and neurosurgery at the David Geffen School of Medicine at UCLA, the researchers plan to test the procedure on several more people beginning this fall at the Ronald Reagan UCLA Medical Center. Those tests will be conducted in partnership with the UCLA Brain Injury Research Center and funded in part by the Dana Foundation and the Tiny Blue Dot Foundation.

If the technology helps other people recovering from coma, Monti said, it could eventually be used to build a portable device -- perhaps incorporated into a helmet -- as a low-cost way to help "wake up" patients, perhaps even those who are in a vegetative or minimally conscious state. Currently, there is almost no effective treatment for such patients, he said.

The study's other co-authors are Vespa, who holds UCLA's Gary L. Brinderson Family Chair in Neurocritical Care and is director of neurocritical care at the Ronald Reagan UCLA

Medical Center; Caroline Schnakers, a UCLA neurosurgery researcher; and Alexander Korb, a Semel Institute researcher.

http://bit.ly/2bTxlJb

High-tech alternative to brain surgery proves effective for most common movement disorder

Researchers exploring focused ultrasound for conditions ranging from breast tumors to Parkinson's

A study published today in the prestigious New England Journal of Medicine offers the most in-depth assessment yet of the safety and effectiveness of a high-tech alternative to brain surgery to treat the uncontrollable shaking caused by the most common movement disorder. And the news is very good.

The paper outlines the results of an international clinical trial, led by Jeff Elias, MD, of the University of Virginia Health System, that evaluated the scalpel-free approach called focused ultrasound for the treatment of essential tremor (ET), a condition that afflicts an estimated 10 million Americans. Not only did the researchers determine that the procedure was safe and effective, they found that it offered a lasting benefit, reducing shaking for trial participants throughout the 12-month study period.

"This study represents a major advance for neurosurgery, treatment of brain disease and specifically the treatment of ET," Elias said. "For the first time in a randomized controlled trial, we have shown that ultrasound can be precisely delivered through the intact human skull to treat a difficult neurological disease."

Pioneering Tremor Trial

The multi-site clinical trial included 76 participants with moderate to severe essential tremor, a condition that often robs people of their ability to write, feed themselves and carry out their normal daily activities.

The trial participants all had tried existing medications, without success. The mean age was 71, and most had suffered with their tremor for many years. Seventy-five percent of participants received the experimental treatment using focused ultrasound guided by magnetic resonance imaging. The remaining 25 percent underwent a sham procedure, to act as the control group. (They would later be given the opportunity to undergo the real procedure.)

Participants who received the treatment showed dramatic improvement, with the beneficial effects continuing throughout the study period. The researchers employed a 32-point scale to assess tremor severity, and they found that mean tremor scores improved by 47 percent at three months and 40 percent at 12 months. Participants reported major improvements in their quality of life. People who couldn't feed themselves soup or cereal could again do so.

Participants who received the sham procedure, on the other hand, showed no significant improvements.

"The degree of tremor control was very good overall in the study, but the most important aspects were the significant gains in disabilities and quality of life - that's what patients really care about," Elias said.

The most commonly reported side effects were gait disturbances and numbness in the hand or face; in most instances, these side effects were temporary but some were permanent.

FDA Approved

Based on the clinical trial led by Elias, the federal Food and Drug Administration has approved the focused ultrasound device, manufactured by InSightec Inc., for the treatment of essential tremor. The device focuses sound waves inside the brain to create heat, much like a magnifying glass focuses light. That heat can then be used to interrupt the troublesome brain connections responsible for the tremor. Elias can actually watch as patients' tremor decreases, and the real-time imaging allows him to zone in on exactly the right spot before making any permanent changes to the brain.

The FDA approval means UVA can make the procedure available to eligible patients. UVA, however, is still working out the necessary logistics; it's not yet clear when Elias will begin treating patients. Because the approach is so new, insurance plans will not yet cover the

procedure, though that may change in the coming months. The cost at UVA has not yet been determined.

People interested in the procedure can learn more at uvahealth.com/focusedultrasound. The site includes a list of frequently asked questions and will be updated as UVA prepares to make the treatment available.

The procedure is not for everyone with essential tremor. It can't be used in patients who cannot undergo MRI imaging, including those with implanted metallic devices such as a pacemaker. It is also not available for pregnant women, people with heart conditions or very high blood pressure, patients with kidney disease or clotting disorders, patients on blood thinners, patients with a history of strokes or brain tumors and people with substance abuse issues. There are other exclusions as well. Doctors at UVA will evaluate potential patients to determine their eligibility and then recommend the best course of treatment.

Groundbreaking Research

UVA is a world leader in focused ultrasound research. Elias and his colleagues are testing the capability of focused ultrasound to treat Parkinson's disease, epilepsy, brain tumors and benign breast tumors.

The essential tremor research has been supported by InSightec, the Focused Ultrasound Foundation and the BIRD (US-Israel Binational Industry Research and Development) Foundation.

http://bit.ly/2bTyi4f

New method developed for producing some metals

Using electricity rather than heat can reduce both energy costs and greenhouse gas emissions

CAMBRIDGE, Mass. -- The MIT researchers were trying to develop a new battery, but it didn't work out that way. Instead, thanks to an unexpected finding in their lab tests, what they discovered was a whole new way of producing the metal antimony -- and potentially a new way of smelting other metals, as well.

The discovery could lead to metal-production systems that are much less expensive and that virtually eliminate the greenhouse gas emissions associated with most traditional metal smelting. Although antimony itself is not a widely used metal, the same principles may also be applied to producing much more abundant and economically important metals such as copper and nickel, the researchers say.

The surprising finding is reported this week in the journal Nature Communications, in a paper by Donald Sadoway, the John F. Elliott Professor of Materials Chemistry; postdoc Huayi Yin; and visiting scholar Brice Chung.

"We were trying to develop a different electrochemistry for a battery," Sadoway explains, as an extension of the variety of chemical formulations for the all-liquid, high temperature storage batteries that his lab has been developing for several years. The different parts of these batteries are composed of molten metals or salts that have different densities and thus inherently form separate layers, much as oil floats on top of water. "We wanted to investigate the utility of putting a second electrolyte between the positive and negative electrodes" of the liquid battery, Sadoway says.

Unexpected results

But the experiment didn't go quite as planned. "We found that when we went to charge this putative battery, we were in fact producing liquid antimony instead of charging the battery," Sadoway says.

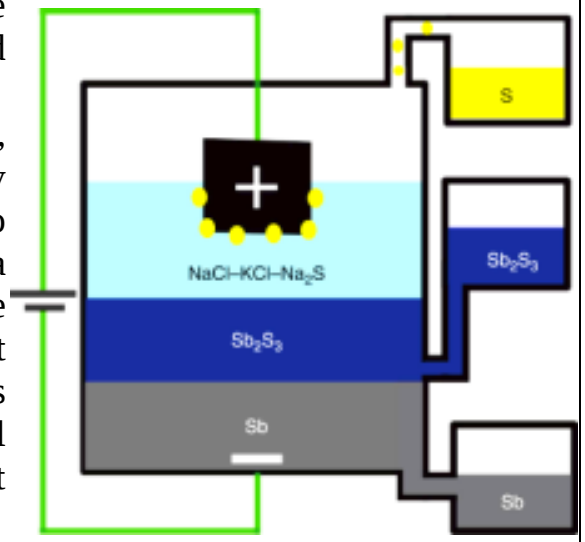
Then, the quest was on to figure out what had just happened.

The material they were using, antimony sulfide, is a molten semiconductor, which normally would not allow for the kind of electrolytic process that is used to produce aluminum and some other metals through the application of an electric current.

"Antimony sulfide is a very good conductor of electrons," Sadoway says. "But if you want to do electrolysis, you only want an ionic conductor" -- that is, a material that is good at conducting molecules that have a net electric charge. But by adding another layer on top of the molten semiconductor, one that is a very good ionic conductor, it turned out the electrolysis process worked very well in this "battery," separating the metal out of the sulfide compound to form a pool of

99.9 percent pure antimony at the bottom of their cell, while pure sulfur gas accumulated at the top, where it could be collected for use as a chemical feedstock.

In typical smelting processes, the sulfur would immediately bond with oxygen in the air to form sulfur dioxide, a significant air pollutant and the major cause of acid rain. But instead this contained process provides highly purified metal without the need to worry about scrubbing out the polluting gas.



Simple, efficient process Schematic of three-layered electrolysis cell.

Schematic of three-layered electrolysis cell.

Schematic illustrating the use of an electron-blocking secondary electrolyte for direct electrolytic conversion of molten semiconducting Sb2S3 into liquid Sb and sulfur vapour.

Electrolysis is much more efficient than traditional heat-based smelting methods, because it is a single-step continuous process, Sadoway explains. The discovery of that process is what transformed aluminum, more than a century ago, from a precious metal more valuable than silver into a widely used inexpensive commodity. If the process could be applied to other common industrial metals such as copper, it would have the potential to significantly lower prices as well as reduce the air pollution and greenhouse gas emissions associated with traditional production.

"The thing that made this such an exciting finding," Sadoway says, "is that we could imagine doing the same for copper and nickel, metals that are used in large quantities." It made sense to start with antimony because it has a much lower melting point -- just 631 degrees Celsius -- compared to copper's 1,085 C. Though the higher melting temperatures of other metals add complication to designing an overall production system, the underlying physical principles are the same, and so such systems should eventually be feasible, he says.

"Antimony was a good test vehicle for the idea, but we could imagine doing something similar for much more common metals," Sadoway says. And while this demonstration used an ore that is a sulfide (metal combined with sulfur), "we see no reason why this approach couldn't be generalized to oxide feedstocks," which represent the other major category of metal ores. Such a process would produce pure oxygen as the secondary product, instead of sulfur.

Ultimately, if steel could be produced by such a process, it could have a major impact, because "steel-making is the number one source of anthropogenic carbon dioxide," the main greenhouse gas, Sadoway says. But that will be a more difficult process to develop because of iron's high melting point of about 1,540 C.

http://bit.ly/2c0BVrd

Newly discovered multicomponent virus is the first of its kind to infect animals

First time a multicomponent virus has been found that is capable of infecting animals

For the first time, a multicomponent virus--which contains different segments of genetic material in separate particles, rather than a single strand of genetic material--has been found that is capable of infecting animals, an international team led by the U.S. Army reports August 25 in Cell Host & Microbe. The Guaico Culex virus (GCXV), a type of Jingmenvirus, was isolated from mosquitoes, and opens up a new avenue of research into potentially infectious agents. The virus does not appear to infect mammals.

"Until now, multicomponent viruses were thought to infect only plants and fungi, as a result of relatively inefficient transmission," says first author Jason Ladner, a staff scientist from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). "Our finding

that these viruses are present in mosquitoes is going to challenge us to re-evaluate some of our assumptions about them."

Multicomponent viruses use a method of transmission that's different from other viruses known to infect animals. Instead of being contained in a single viral particle, their genomes are segmented and encapsulated among multiple particles. A yellow fever virus, for example, has all its genetic material packaged into a single particle. Therefore, one particle is enough to infect a cell. But in order for a multicomponent virus to establish an infection, the cell has to get infected with at least one particle of each type.

The research is part of a global effort to monitor and prepare for outbreaks of unknown viral diseases. Mosquitoes and other insects can act as vectors for viral diseases, carrying them from place to place and transmitting them to human hosts via bites. Although the new virus does not appear to be a human pathogen, or even a mammalian one, the investigators say this work is a good exercise to help hone the tools and expertise needed to characterize novel infectious agents.

In the study, the USAMRIID researchers worked with several other teams, including groups from the University of Texas Medical Branch and the New York State Department of Health, to isolate mosquitoes from different regions around the world. The newly discovered virus is named Guaico Culex after the Guaico region of Trinidad in which the mosquitoes that contained it were found.

Guaico Culex was isolated by growing material obtained from the mosquitoes in cell culture. "This method has been useful particularly in finding new arboviruses, which are transmitted by mosquitoes and other arthropods to mammals," Ladner says. To identify arboviruses, cultures of mammalian cells are used. "We were also interested in viruses that may be found within mosquitoes but don't necessarily grow on mammalian cells, so we used cultures of insect cells, enabling us to find this new virus."

Deep sequencing indicated that Guaico Culex belongs to a group of segmented viruses called Jingmenviruses, which were first discovered in 2014. In collaboration with a group at the University of Wisconsin-Madison, the USAMRIID researchers also showed for the first time evidence of a Jingmenvirus in the blood of a non-human primate, in this case a Ugandan red colobus monkey. This finding is also published in the current Cell Host & Microbe paper.

Experts believe that the most likely infectious viruses to make the jump to humans are those that are already circulating in other mammals, especially non-human primates. Phylogenetic analysis indicated that this monkey virus shared a segmented common ancestor with Guaico Culex. However, researchers don't yet know if all Jingmenviruses are multicomponent like the Guaico Culex virus. It is also not known whether the Jingmenvirus isolated from the monkey had a pathogenic effect.

"One of the things we're focused on at USAMRIID is rapid identification of pathogens from both clinical and environmental samples as well as characterization of novel viruses," says Gustavo Palacios, Director of the Center for Genome Sciences at USAMRIID and the study's senior author. "We're trying to make sure that we're not blindsided when the next virus comes around. With all of the diversity seen in these emerging viruses, we never know what the next one will be to have an impact on human health."

This research was supported by the Defense Threat Reduction Agency, the National Institutes of Health, the James W. McLaughlin endowment fund, a Smithsonian Tropical Research Institute-Environmental Protection Agency grant, and a Robert E. Shope fellowship.

Cell Host & Microbe, Ladner et al: "A Multicomponent Animal Virus Isolated from Mosquitoes" http://www.cell.com/cell-host-microbe/fulltext/S1931-3128(16)30310-9

http://bit.ly/2bmRh9S

Insights on lung micro-environment explain why cancer spreads to the lungs

Discovery could help overcome metastasis as major obstacle to curative treatment

COLUMBUS, Ohio - The same mechanisms that that prevent people from having an inflammatory response to harmless environmental exposures in day-to-day life could also all allow rogue cancer cells to

spread to the lungs, according to new research from The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James).

Researchers have discovered and described how the lung's unique underlying immune environment enables cancer to readily spread to the organ.

They report their findings online ahead of print in the scientific journal, Cell, on Aug. 25, 2016.

Cancer cells must break through normal immune defenses in order to spread to other parts of the body. Little is known, however, about the mechanisms that lead to cancer's spread to the lungs.

Nearly 90 percent of cancer deaths occur when cancer spreads to a different part of the body -presenting a major obstacle to curative treatment.

The lungs are a common site of metastasis for primary bladder, breast, colon, kidney, melanoma, ovary, pancreas, bone, rectal, stomach, thyroid, uterine and lung cancer.

In this new study, researchers describe how oxygen functions as an immune system checkpoint to create an environment that enables cancer's spread to the lung more easily.

"Every time we take a breath, we bring things into our lungs that could produce a pretty dramatic and potentially harmful immune response - but the majority of the time they don't because in a normal, healthy state our immune systems are set up to accommodate for this," explains David Clever, PhD, first author of the manuscript and a current medical student at Ohio State.

Clever completed this research under the mentorship of Nicholas Restifo, MD, of National Cancer Institute (NCI) during the doctoral portion of his Medical Scientist Training Program.

"The same 'normal' mechanisms put in place to suppress immune responses against harmless material taken into the body during the act of breathing can also suppress immune responses to the colonizing cancer cells that lead to metastatic tumors in the lungs. This creates an immunologically favorable niche - meaning the environment is prime for cancer cells to slip through the immune system's defenses, thrive and grow in the lungs."

Specifically, the team discovered that certain oxygen-sensing proteins (PHD cells) function to limit inflammation by T cells, a type of immune cell capable of killing cancer cells.

In the highly oxygenated lung microenvironment the oxygen-sensing PHD proteins limit immune responses against cancer cells which opens the lung up as a a fertile ground for metastasis.

Researchers found that by blocking the PHD proteins -- using either pharmacologic agents or mice bred to have the PHD proteins "knocked-out" of their T cells -- they could enhance T-cell responses against cancer and limit metastasis to the lung.

These results contribute a new immunological basis for the predisposition of many cancers to metastasize to the lung that could help scientists develop new therapies to prevent the spread of cancer to the lungs.

"Adoptive cell transfer immunotherapy provides a unique opportunity for manipulation of a patient's own T cells out of the body," said Restifo.

"Although our finding is in mice, we are eager to test whether disruption of the oxygen sensing machinery in T cells -- with drugs, genetics, or regulation of environmental oxygen -- will enhance the efficacy of T-cell mediated immune therapies for cancer in humans."

The study was funded by NCI and National Institute of Allergy and Infectious Diseases (NIAID) and with charitable gifts from Li Jinyuan, The Tiens Charitable Foundation and The Milstein Family Foundation. Additional support was provided by The Wellcome Trust/Royal Society and The UK Biotechnology and Biological Sciences Research Council.

Collaborators in this study include Rahul Roychoudhuri, Madhusudhanan Sukumar, Christopher Klebanoff, Robert Eli, Zhiya Yu, Jenny Pan, Douglas Palmer, and Luca Gattinoni of NCI; Michael Constantinides, Michael Askenase, Heather Hickman and Yasmine Belkaid of NIAD; and Anthony Phan, John Goulding and Ananda Goldrath of the University of California.

http://bit.ly/2bmV0nO

Experts say inexpensive drug could slow heart disease for type 1 diabetic patients

Scientists at Newcastle University believe a drug commonly prescribed for Type 2 diabetes could be routinely taken by Type 1 diabetic patients to slow the development or delay heart disease.

Metformin is an inexpensive treatment that is often used for Type 2 diabetes to lower blood sugar levels by reducing glucose production in the liver.

The drug is not regularly given to patients with Type 1 diabetes. However, for the first time, a clinical trial has revealed metformin can promote a patient's ability to repair their own damaged blood vessels by increasing vascular stem cells.

Heart disease is the leading cause of illness in diabetic patients, accounting for more than half of all fatalities. Metformin may be used to lower Type 1 diabetic patients' risk of developing this complication.

Findings of the clinical trial are published today in the journal, Cardiovascular Diabetology. This follows previous laboratory work at Newcastle University which explored the mechanism behind metformin.

Dr Jolanta Weaver, Senior Lecturer in Diabetes Medicine at Newcastle University and Honorary Consultant Diabetologist at Queen Elizabeth Hospital, Gateshead, led both studies.

She believes this new research is a major development in understanding the best ways to further improve treatment in Type 1 diabetes.

Dr Weaver said: "As the outcomes of heart disease is worse in diabetic versus non-diabetic patients, there is a need to identify additional treatment options.

"Metformin could routinely be used by patients with Type 1 diabetes to help lower their chances of developing heart disease, by increasing a repair mechanism created by vascular stem cells released from the bone marrow.

"Our research is an exciting step forward as it may have positive clinical implications for patients with increased risk of cardiovascular disease by improving their treatment options.

"For the first time, this study has shown metformin has additional benefit beyond improving diabetes control when given to patients with relatively well controlled Type 1 diabetes.

"We have established the drug increases patients own vascular stem cells, which will help delay or slowdown heart disease.

"Our findings also show that the cells associated with damaged blood vessels were reduced, confirming that the repair of blood vessels was taking place in our patients."

Researchers studied a treatment group of 23 people aged 19-64 who had Type 1 diabetes for up to 23 years and had no evidence of heart disease.

Patients were given metformin at a dose they could tolerate, between one to three tablets a day, for eight weeks. Participants were advised to adjust their insulin to keep blood glucose levels safe.

Scientists measured patients' stem cells directly in the blood and also grew stem cells in a test tube, observing how they behaved. Another cell type was also counted to assess damaged blood vessels.

The participants were matched with nine patients within the same age bracket who took standard insulin treatment and 23 healthy non-diabetic people aged 20-64.

Experts found that the stem cells of patients who took metformin were able to promote the repair of the blood vessels and there was an improvement in how vascular stem cells worked.

Type 1 diabetes is a lifelong autoimmune condition that develops when the pancreas does not produce any insulin, causing a person's blood sugar level to become too high. It is estimated around 400,000 people in the UK have the condition.

Dr Weaver said: "We have shown that all our patients in the study had their insulin doses reduced after taking metformin and have not suffered any serious adverse effect.

"Patients with Type 1 diabetes may wish to consider discussing with their GP the possibility of adding metformin, even at a very low dose, to the insulin that they are taking. However, care needs to be taken to adjust insulin dose to prevent too low glucose levels."

A pilot study was funded by Diabetes Research and Wellness Foundation and the extended study was financially supported by the Diabetes Research Fund in Gateshead.

Dr Eleanor Kennedy, Research Manager at Diabetes Research and Wellness Foundation, said: "The Diabetes Research and Wellness Foundation is delighted to have funded the initial pilot study that led Dr Weaver and her colleagues to conduct this small clinical trial.

"The results, which indicate that metformin, a drug commonly used in the treatment of Type 2 diabetes, could also have a powerful effect in people with Type 1 diabetes is unexpected.

"We hope that these results can lead to a much larger clinical trial."

Case study

Quantity surveyor Alex Laws was part of the Newcastle University clinical trial and is delighted with the results of the study.

The 31-year-old, of Gateshead, was diagnosed with Type 1 diabetes at the age of just seven and has good control of her condition. She was enrolled on the clinical trial in the summer of 2013.

Alex said: "I was keen to be part of the clinical trial as I know how important research is into helping people with the condition - I previously worked in the medical research field.

"People with Type 1 diabetes can suffer from a number of complications, especially in the long-term, so it's important as much as possible is done to limit serious problems.

"Heart disease is a concern for people with Type 1 diabetes so any treatment that can help with this and give an advantage to the patient is a good thing."

Metformin improves circulating endothelial cells and endothelial progenitor cells in Type 1 diabetes: MERIT Study Fahad W Ahmed, Rachel Rider, Michael Glanville, Kilimangalam Narayanan, Salman Razvi and Jolanta U Weaver. Cardiovascular Diabetology. DOI: 10.1186/s12933-016-0413-6

http://bit.ly/2c1qqVR

Whisper tech turns secrets into normal speech

Beware eavesdropping software

By Bas den Hond

PSST! Did you hear the news? A new program can convert whispers into normal-sounding speech.

Whispering is useful if you don't want to be overheard, but it's also unavoidable if your vocal cords are damaged. So an app that turns whispered words into full speech could be invaluable. One hurdle is that whispering cannot produce all the tones achieved by our vocal cords. That missing ingredient means it doesn't have an actual pitch.

Any app that miscalculates the pitch can muddle the message. In English, pitch makes the difference between sounding earnest and sarcastic. In Japanese, it changes the meaning of words, for example turning "good" into "drunkenness".

For this reason, whisperers instinctively try to indicate the pitch in other ways, for example by changing the shape of their mouth, helping listeners guess the intended pitch.

"A miscalculated pitch can muddle the message. It can change the Japanese word 'good' to 'drunkenness'"

Hideaki Konno and his colleagues at Hokkaido University of Education in Japan played sounds with just one frequency to five people and asked them to whisper at those pitches. This established a link between their whispers and intended pitch (Speech Communication, doi.org/bn8z).

From that, the team built a pitch predictor. The algorithm analysed whispered Japanese words for which pitch changes meaning, then added the missing frequency. Eight people who listened to the synthesised words grasped the intended meaning 72 per cent of the time.

Such a system could eventually run on a smartphone, says Konno. But for that to happen, the algorithm must become good enough to reconstruct complete sentences.

http://www.medscape.com/viewarticle/867772

Paul Offit Responds to News About HPV Vaccine 'Syndrome'

Response to "Chronic Symptoms After HPV Vaccine: Part of Wider Syndrome?"

Paul A. Offit, MD

To the Editor:

I am writing from the Vaccine Education Center at the Children's Hospital of Philadelphia, in response to a *Medscape Medical News* article published on August 11, 2016, titled "Chronic Symptoms After HPV Vaccine: Part of Wider Syndrome?" This news article covered a study by an Italian group that was recently published in *Immunologic Research*.[1] This notion that the HPV vaccine can cause symptoms of chronic fatigue or fibromyalgia has been out there for years. And frankly, it's the reason that the Ministry of Health in Japan has decided not to recommend the HPV vaccine, which is sad because this issue has been looked at again and again.

First of all, the HPV vaccine was studied for safety in 30,000 people for 7 years before licensure.[2] It has been formally studied both in phase 4 postlicensure studies and by the Vaccine Safety Datalink in more than a million people, and has been found not to cause chronic fatigue or fibromyalgia. When those symptoms do occur, they occur at the *same rate* in both vaccinated and unvaccinated groups.[3]

We learned from these studies that the HPV vaccine doesn't prevent fibromyalgia or chronic fatigue in adolescents. That Medscape chose to highlight this article,[1] as if it were in any way an advance, is disappointing. Frankly, this falls under the same category as the syndrome described by Andrew Wakefield—that the MMR vaccine caused intestinal symptoms and autism, which also was thoroughly debunked.[4]

The problem is that this raises the same ill-founded belief that was raised by Katie Couric on her show *Katie* that the HPV vaccine may cause chronic symptoms. As a consequence, at least a segment of society has become falsely concerned about the safety of this vaccine. We know that the HPV vaccine doesn't cause these problems, but people are making the choice not to have their children receive the vaccine; only 40% of girls and about 21% of boys are getting this vaccine.[5]

Every year in this country, the HPV-9 [vaccine] would prevent about 29,000 cases of cancer—two thirds in girls, about one third in boys—and it would prevent about 4800 deaths.[6] So when only 40% of girls and 21% of boys are getting this vaccine, we can assume that about 2000 children every year in this country are going to become adults who die, needlessly, from this infection.

I think we have scared people unnecessarily, in part because we have been a little concerned about bringing up the issue of sex in front of these children (and that can be uncomfortable), instead of just talking about what we should talk about: that this is a cancer-preventing vaccine that's being underutilized. So, I'm a little disappointed that Medscape chose, in any sense, to highlight an article claiming that the HPV vaccine caused chronic disease when such a claim is without basis. Thank you.

References

1. Palmieri B, Poddighe D, Vadala M, Laurino C, Carnovale C, Clementi E. Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature. Immunol Res. 2016 Aug 9. [Epub ahead of print]

2. Centers for Disease Control and Prevention. Human Papillomavirus (HPV) Vaccine Safety. http://www.cdc.gov/vaccinesafety/vaccines/hpv-vaccine.html Accessed August 22, 2016.

3. Centers for Disease Control and Prevention. Frequently Asked Questions About HPV Vaccine Safety. http://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html#A5 Accessed August 22, 2016.

4. Godlee F, Smith J, Marcovitch H. Wakefield's article linking MMR vaccine and autism was fraudulent. BMJ. 2011;342:c7452.

5. Centers for Disease Control and Prevention. Teen Vaccination Coverage. http://www.cdc.gov/vaccines/parents/vacc-coverage-teens.html Accessed August 22, 2016.

6. Centers for Disease Control and Prevention, Communication and Education Branch, National Center for Immunization and Respiratory Diseases. Human Papillomavirus. The Pink Book. 2015. http://www.cdc.gov/vaccines/pubs/pinkbook/hpv.html Accessed August 22, 2016.

http://bit.ly/2bKq8xR

Researchers Are Building a Tear Bank to Better Understand Why We Weep

Scientists will eventually be able to select tears by age and gender from the cryogenic repository

By Noah Caldwell on September 1, 2016

Compared with other bodily excretions, tears are vastly understudied. Collecting the salty drops is tedious—weepy donors are rare, men hardly ever sign up and tears must be "fresh" for their makeup to be properly analyzed. As a result, researchers lack a consensus about the purpose of a basic human behavior. Is crying a primal way to communicate that many species share, as some chemists hypothesize? Or is it, as psychologists have put forth, a uniquely human key to social bonding? Israeli neurobiologist Noam Sobel has a plan to advance the field: he has perfected a way to flash-freeze tears and is now working to create a "tear bank" for researchers around the world.

Sobel, who is based at the Weizmann Institute of Science in Rehovot, discovered in 2011 that women's tears contain pheromones that lower the testosterone levels of nearby men. But building on that research has been slow because the molecules easily degrade.

To keep the chemical composition of tears intact, Sobel and his team have developed a way to systematically freeze the droplets. The method involves liquid nitrogen, which rapidly lowers the temperature of a sample below −80 degrees Celsius. The process preserves most of the tears' chemicals, say the researchers, who plan to publish their results later this year. Next they will start building a cryogenic repository of tears, categorized by source and orderable online. "Just as other biobanks exist for amniotic fluid, blood and urine, we'll have a biobank of tears," Sobel says. "This would let you do studies in two weeks instead of six months."

A tear bank for research "has tremendous possibilities," says Saad Bhamla, a bioengineer at Stanford University who often has to use animal tears in his own investigations into how tears create a film on the eye. As examples of applications, he points to Silicon Valley's interest in contact lenses that double as a heads-up display, among other functions, and the rising cases of dry eyes from prolonged sessions of staring at a computer screen.

Sobel hopes interested researchers will eventually be able to select tears by age and gender from the repository—say, 200 samples from white males, 18 to 25 years old. This customized access could expedite experiments tackling the chemistry of crying's many unanswered questions: Do tears affect mood or appetite? Do the tears of men and women differ? How do emotional and nonemotional tears—from, say, cutting onions—compare? For Sobel, the more people who cry their eyes out, the better.

http://bit.ly/2bth92f

New oral anticoagulants provide same stroke prevention as warfarin but cause less bleeding

Stroke and arrhythmia: Life or death

Rome, Italy - The new oral anticoagulants provide the same stroke prevention as warfarin but cause less intracranial bleeding, reports an observational study in more than 43 000 patients presented at ESC Congress 2016 today by Dr Laila Staerk, a research fellow at Herlev and Gentofte University Hospital, Denmark.

"Atrial fibrillation is the most common cardiac rhythm disorder and currently affects more than 10 million Europeans," said Dr Staerk.

"Atrial fibrillation is associated with a five-fold risk of stroke, potentially leading to disability and death," continued Dr Staerk. "In the next four decades, the number of patients with atrial fibrillation is expected to triple so the number of Europeans diagnosed could rise to a staggering 25 to 30 million."

Patients with atrial fibrillation are treated life-long with oral anticoagulation to reduce their risk of stroke. But treatment with non-vitamin K antagonist oral anticoagulants (NOACs) and vitamin K antagonists (warfarin) is a double-edged sword, because it lowers the

risk of stroke at the cost of increased bleeding risk. Intracranial bleeding is a particular fear.

With several treatment options available the clinical question of which one to use has often been asked. Dr Staerk said: "There has been a need to investigate safety and effectiveness of NOACs versus warfarin in a 'real world' population and our Danish registries provide this opportunity."

The current study compared the risk of stroke and intracranial bleeding with NOACs (dabigatran, rivaroxaban and apixaban) versus warfarin in a 'real world' setting. The study was conducted at The Cardiovascular Research Centre at Herlev and Gentofte University Hospital in Denmark. It included 43 299 patients with atrial fibrillation who were recruited from Danish nationwide administrative registries.

Some 42% of patients were taking warfarin, while 29%, 16% and 13% were taking dabigatran, apixaban and rivaroxaban, respectively. During follow up, stroke occurred in 1054 patients and there were 261 intracranial bleedings. The researchers found that the risk of having a stroke within one year was similar between the NOAC and warfarin groups, and ranged from 2.0 to 2.5%. At one year the risk of intracranial bleeding was significantly lower in patients treated with dabigatran and apixaban (0.3 to 0.4%) compared to those treated with warfarin (0.6%) (figure 1).

Dr Staerk said: "The inclusion and exclusion criteria in our study were broadly similar for patients initiating NOACs or warfarin, and this gave a straightforward opportunity to directly compare the treatment regimens, which is in contrast to the randomised trials. The results suggest that although they have similar effects in preventing stroke, dabigatran and apixaban were associated with a safer use regarding the absolute one-year risk of intracranial bleeding."

She added: "Our results complement the large randomised phase III trials by providing 'real world' data on stroke and intracranial bleeding with NOACs versus warfarin since fragile patients were not excluded from our nationwide cohort. For example, patients with increased risk of bleeding, liver disease, and chronic kidney disease are less represented in trials."

Dr Staerk concluded: "Registry studies have some limitations such as the observational design, residual confounding, and confounding by drug indication. In the future it would be exciting to see a head-to-head randomised trial performed to compare the different NOAC treatments in patients with atrial fibrillation."

Facts about atrial fibrillation and oral anticoagulants:

Atrial fibrillation is the most common cardiac arrhythmia with an increasing prevalence.

In the next four decades, the number of patients with atrial fibrillation is expected to triple.

Atrial fibrillation is associated with a five-fold risk of stroke, potentially leading to disability and death.

Patients with atrial fibrillation are treated life-long with oral anticoagulation to prevent stroke and death, but oral anticoagulation treatment imposes an increased risk of bleeding.

Sources of funding: The study was supported by Velux Foundations.

http://bit.ly/2c1cWRY

Traffic accidents increased by 50 percent in patients with implantable cardioverter defibrillator

Preventing sudden death -- diet or device

Rome, Italy - The risk of traffic accidents is increased by 50% in patients with an implantable cardioverter defibrillator (ICD) compared to age and gender matched controls, according to a Danish nationwide registry study presented at ESC Congress 2016 today.1

"Driving after ICD implantation is an area of great debate and concern for both doctors and patients," said lead author Dr Jenny Bjerre, a physician at Herlev and Gentofte University Hospital, Copenhagen, Denmark. "Our study provides contemporary data suggesting that the risk of motor vehicle accidents is in fact increased following ICD implantation when compared to controls."

ICDs are widely used to prevent sudden cardiac death in patients with an increased risk of life-threatening arrhythmias (primary prevention) and in patients who have survived a life-threatening arrhythmia, including cardiac arrest (secondary prevention). The number of ICD implantations has increased dramatically over the past decades, now reaching almost 100 000 yearly implants in ESC member countries.

Due to the risk of arrhythmias and potential loss of consciousness while driving, patients with an ICD are temporarily restricted from driving following ICD implantation and/or ICD shock. However, contemporary data to support these recommendations are lacking and the restrictions have a negative influence on patients' quality of life.

The study by Dr Bjerre and colleagues was conducted at The Cardiovascular Research Centre at Herlev and Gentofte University Hospital in Denmark. Using nationwide registers, the researchers identified all Danish residents who received a first ICD for primary or secondary prevention between 2008 and mid-2012. Motor vehicle accidents were recorded from nationwide registers on accidents and deaths.

The study included 4874 ICD patients and a control group of 9748 subjects matched by age and gender. Participants were 63 years old on average.

During an average follow-up period of 2.5 years, 2.3% of ICD patients were in contact with a hospital following a motor vehicle accident, compared to only 1.7% of the control population. Over time, this translated into a 51% increased risk of motor vehicle accidents in ICD patients compared to controls. There was no detectable difference in accident risk between primary and secondary prevention ICD patients.

Although higher than in the control population, the overall rate of motor vehicle accidents in ICD patients was low (1.0 to 1.4% within the first year after implantation), and the researchers observed no deaths due to motor vehicle accidents in patients with an ICD.

Dr Bjerre said: "To date, driving recommendations for ICD patients are based on data from small studies in a few highly selected patients. The Danish nationwide registers provided a unique opportunity to investigate the subject in a 'real world' ICD population."

"Due to the retrospective nature of the study we are unable to conclude that ICDs cause traffic accidents," continued Dr Bjerre. "However, because the control population was generally healthier and took fewer medically prescribed drugs, we speculate that the observed increased risk of motor vehicle accidents in the ICD population is likely a consequence of the underlying cardiovascular disease, rather than the ICD device itself."

Sources of funding: The study was supported by The Arvid Nilsson Foundation and Danish Heart Foundation.

http://apne.ws/2bvXZp5

Playing with sports concussion doubles recovery time: Study

Continuing to play despite a concussion doubles recovery time for teen athletes and leads to worse short-term mental function than in those immediately removed from action, a study found.

By LINDSEY TANNER AP Medical Writer

CHICAGO (AP) -- It's billed as the first to compare recovery outcomes for athletes removed from a game or practice compared with those who aren't. The study was small, involving 69 teens treated at a University of Pittsburgh Medical Center concussion clinic, but the results bolster evidence supporting the growing number of return-to-play laws and policies nationwide

The study was published Monday in the journal Pediatrics.

Keeping Score

The study involved athletes aged 15 on average from several sports, including football, soccer, ice hockey and basketball who had concussions during a game or practice. Half continued to play and took 44 days on average to recover from symptoms, versus 22 days in those who were immediately sidelined.

Sidelined players reported symptoms immediately, including dizziness, headaches, mental fogginess and fatigue, and were diagnosed with

concussions by trainers or team physicians. The others, who continued playing for 19 minutes on average, delayed reporting symptoms and were diagnosed later.

Those who continued to play had worse scores on mental function tests performed eight days after the concussion and 30 days after the concussion. Medical records showed mental function had been similar in all players before their concussions.

Risky Returns

Return-to-play policies are widespread, especially in youth athletics, and they typically recommend sidelining players after a suspected concussion until symptoms resolve. One of the main reasons is to prevent a rare condition called second-impact syndrome - potentially fatal brain swelling or bleeding that can occur when a player still recovering from a concussion gets hit again in the head.

The study results show that a prolonged recovery is another important risk from returning to play too soon - one that "no one had really calculated" until now, said Dr. Allen Sills, a Vanderbilt University neurosurgeon. He was not involved in the research.

Not Reported

About 300,000 sports-related concussions occur each year nationwide among all ages. In high school athletics, they occur at a rate of almost 3 per 10,000 games or practices.

Evidence suggests up to 50 percent of concussions in teen sports aren't reported. Athletes are sometimes not aware they've experienced a concussion, or they suspect a head injury but continue playing because "they don't want to let their teammates down," said University of Arkansas concussion researcher R.J. Elbin, the study's lead author.

The results "give us more ammunition" to persuade young athletes to heed the return-to-play advice, Elbin said.